

# The Antiseptic

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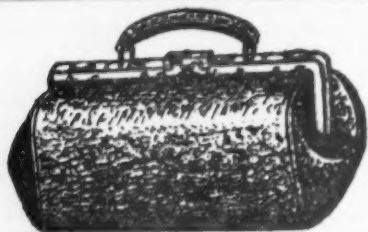
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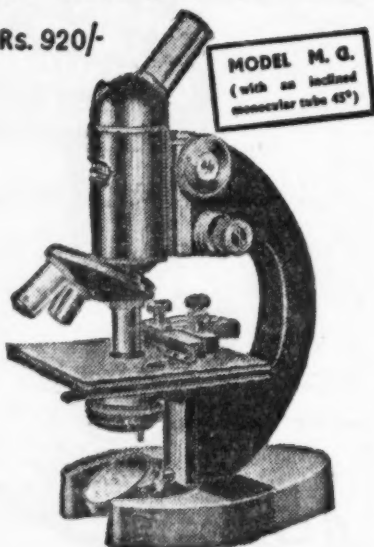
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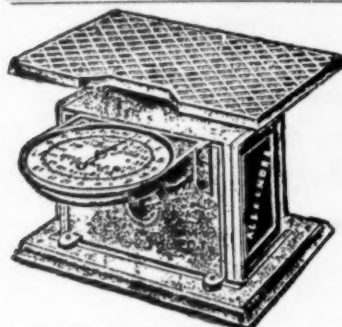


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SETS THE  
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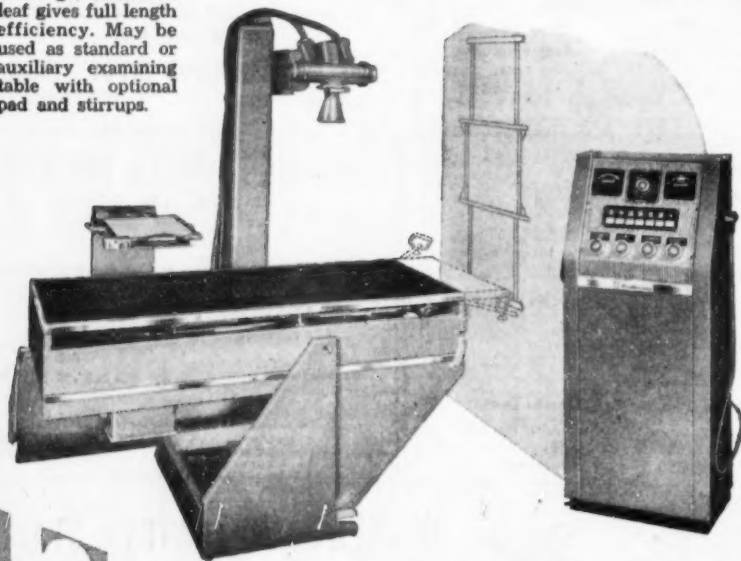
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RADIOGRAPHIC AND  
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Includes (1) All-automatic push-button control (2) Electronic timer (3) Double focus 100 MA tube head (4) Separate fluoroscopic tube head (5) 12 x 16 Patterson B-2 screen (6) L-F Bucky.

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# Sulfotropine

COMBINATION OF SULPHANILAMIDE &amp; HEXAMETHYLENETETRAMINE

Disinfectant of the urinary &amp; biliary ducts.

*Packings:* Tubes of 24 & 100 Tablets*Ampoules:* Boxes of 5 x 5 c.c. & 25 x 5 c.c.

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BRAND OF OXYTETRACYCLINE

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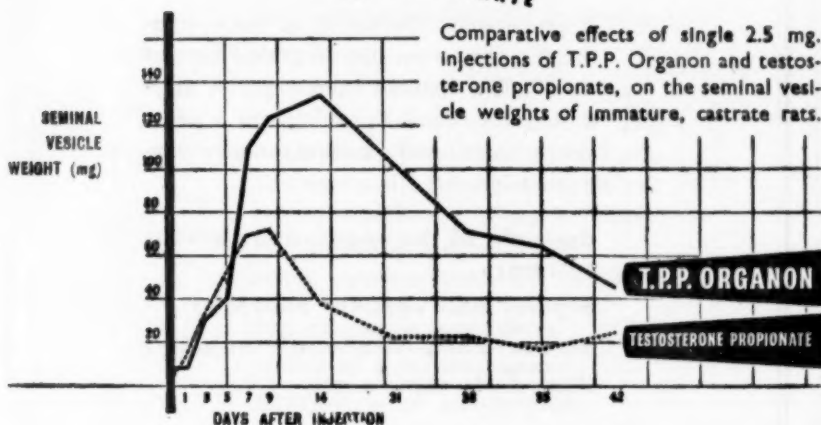
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TESTOSTERONE  
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- LONGER ACTING AND MUCH MORE POTENT THAN TESTOSTERONE PROPIONATE
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A combination containing as the sympatholytic component the hydrated form of an alkaloid isolated from ergot — dihydroergocristine — in addition to a para-sympatholytic and a central sedative component indicated in

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## with Vitamin B Complex

The haematopoietic tonic combining  
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vitamin B<sub>1</sub> (thiamine) 16.7 mg. in 100 gm.  
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nicotinamide 67 mg. in 100 gm.  
calcium pantothenate 10 mg. in 100 gm.  
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**For anaemic conditions  
delayed convalescence  
conditions of exhaustion**

Packing: Bottles of approx. 180 gm. (5 1/4 fl. ozs.)



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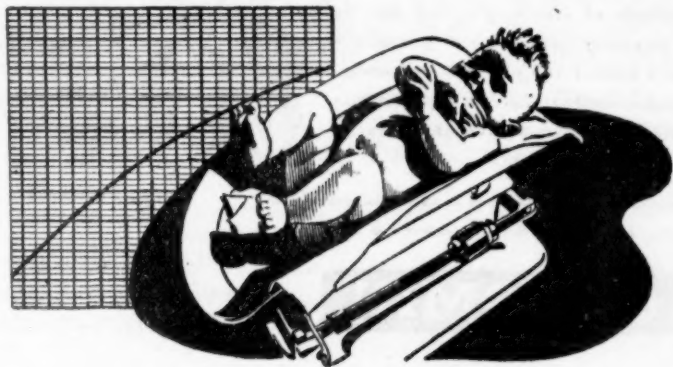
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Easily digested, containing a reduced (but invariable) fat ration, ELEDON has the advantage of providing sufficient calories to form a most satisfactory diet. And this over a long unbroken period, without risk of malnutrition of A avitaminosis.

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Even in these enlightened days, guidance on methods of family planning can do much to remove anxiety and promote a patient's mental and physical well-being. Gynomin entirely fulfils the requirements of a modern contraceptive and may be accepted with confidence.



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*The scientifically balanced  
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Vitamin B<sub>12</sub> potentiated by folic acid  
for the treatment of Megaloblastic Anaemia and Sprue

## 'ANAFOLIN'

Where the marrow is megaloblastic, both folic acid and Vitamin B<sub>12</sub> are necessary to re-establish normal erythropoiesis.

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ANAFOLIN presents the essential factors folic acid and Vitamin B<sub>12</sub> in balanced proportions for parenteral and oral administration.



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**A FUNDAMENTAL ADVANCE  
IN SENNA THERAPY**

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**CHOCOLATE  
LAXATIVE GRANULES**

For the first time a standardised preparation of senna has been evolved which retains the full laxative activity of the pod. (*J. Pharm. Pharmacol.*, 1950, 2, 813.)

Thus a new field of usefulness has been opened up for one of the safest and most physiological of laxatives.

SENOKOT is in granule form; it contains cocoa, malt and sugar, has a delicious taste and is very economical.

SENOKOT is tested chemically and biologically and is completely dependable.

SENOKOT is not advertised to the public and may be prescribed.

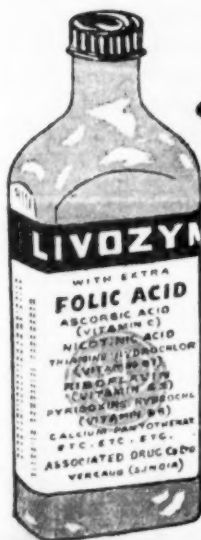


Supplied in 2 oz. tins (approximately 26 teaspoonfuls)  
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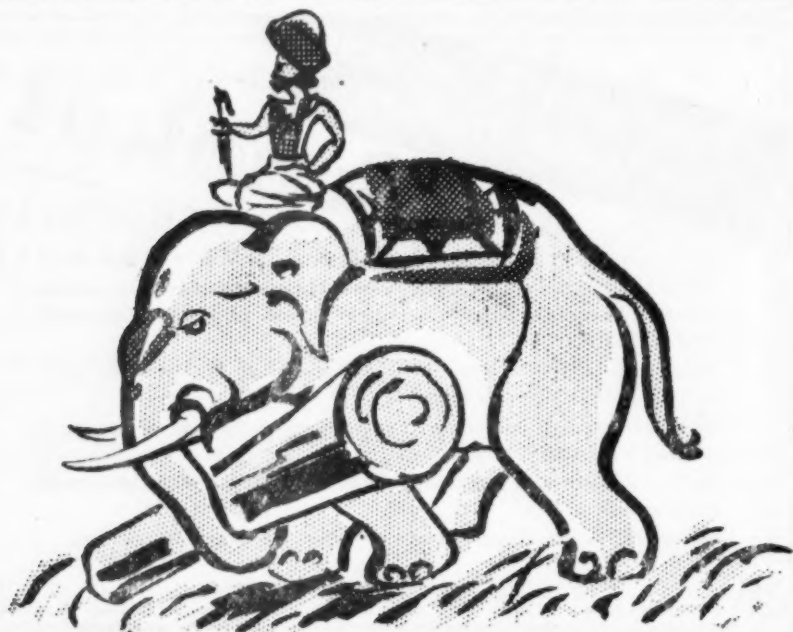
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WITH EXTRA  
**FOLIC ACID**  
IS A MODIFIED

Non-Ferruginous Form of the Nutritive, Nutrition-Promoting, Non-Alcoholic and Restorative Tonic, **LIVOZYME**, fortified with Extra Folic Acid, Riboflavin, Calcium Pantothenate Pyridoxine Hydrochloride and Ascorbic Acid (Vitamin C).

Possessing enhanced Haemopoietic action in Nutritional Macrocytic Anæmias and an enhanced repairing and tonic effect on the Neuro-Muscular Mechanism of the Gastro-Intestinal Tract in Sprue Syndrome.

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**AMPHOTERIC GEL**

Available in 12 oz. bottles and in boxes  
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# VITAMINS

As a medical man you  
will be pleased to  
know that the vitamins  
added to Parle's  
GLUCO Biscuits come  
from the famous  
Swiss laboratory.

## LABORATORY REPORT

Here is the Report dated 15-5-'52 of the  
Hoffmann-La Roche Laboratories on the  
analysis of Parle's Vitamin-enriched  
GlucO Biscuits:

Vitamin B <sub>1</sub>	•	1.56 mg. per lb.
Vitamin B <sub>2</sub>	•	1.12 mg. per lb.
Niacin	•	16.8 mg. per lb.



*Parle's*  
**GlucO BISCUITS**  
★ ENRICHED WITH VITAMINS



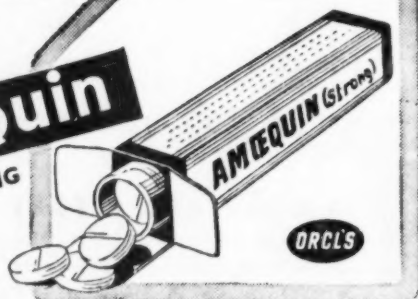
of proved value in acute and chronic  
amoebiasis, as well as in lamblasis and  
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Each tablet contains  
Iodo-chloro-hydroxy-  
quinoline  $2\frac{1}{2}$  grs  
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Excipients 1 gr

**amœquin**  
STRONG

THE ORIENTAL RESEARCH &  
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


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*restores nitrogen equilibrium*



The negative nitrogen   
balance in illness leads to breakdown  
and excretion of body proteins  
like those of the muscles; the patient  
gets thinner every day.

**HI-NUTRON** restores the nitrogen  
equilibrium  preventing waste  
during illness and aiding convalescence.

**HI-NUTRON** contains  
the protein 'Myosin' which provides  
all the essential amino acids.

Ampoules of 5 and 10 cc.

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## for expectant and nursing mothers

Made from full-cream fresh milk and the nutritive extracts of wheat and malted barley, Horlicks forms an excellent addition to the diet of expectant and nursing mothers.

Physiological tests have shown that Horlicks has a definite anti-ketogenic value; that its proteins are promptly digested and absorbed, and that its carbohydrates are remarkably well tolerated and utilised. Clinical experience confirms these tests. If it is taken regularly during pregnancy Horlicks helps to prevent and relieve morning sickness. Many mothers who have previously failed to breast feed their babies have been able to do so after taking Horlicks regularly. It is the opinion of many doctors and nurses that Horlicks ensures a regular supply of breast milk.

## HORLICKS

**PRESCRIBED WITH CONFIDENCE FOR OVER SEVENTY YEARS**

HL 3773

# Ergoapiol-(Smith)

## A Menstrual Regulator . . .

When the periods are irregular, due to constitutional causes, ERGOAPIOL (Smith) is a reliable prescription. Containing apiol (M.H.S. special) together with ergot and oil of savin of the highest quality, this preparation effectively stimulates uterine tone and controls menstrual and postpartum bleeding.

In cases of **Amenorrhea, Dysmenorrhea, Menorrhagia and Metrorrhagia**.

**hagia**, Ergoapiol serves as a good uterine tonic and hemostatic. Valuable in obstetrics after delivery of the child.

**DOSAGE:** 1 to 2 capsules 3 or 4 times daily. Supplied only in packages of 20 capsules. Literature on request.

As a safeguard against imposition the letters MHS are embossed on the inner surface of each capsule, visible only when the capsule is cut in half as shown.

**MARTIN H. SMITH COMPANY**  
NEW YORK, N.Y.

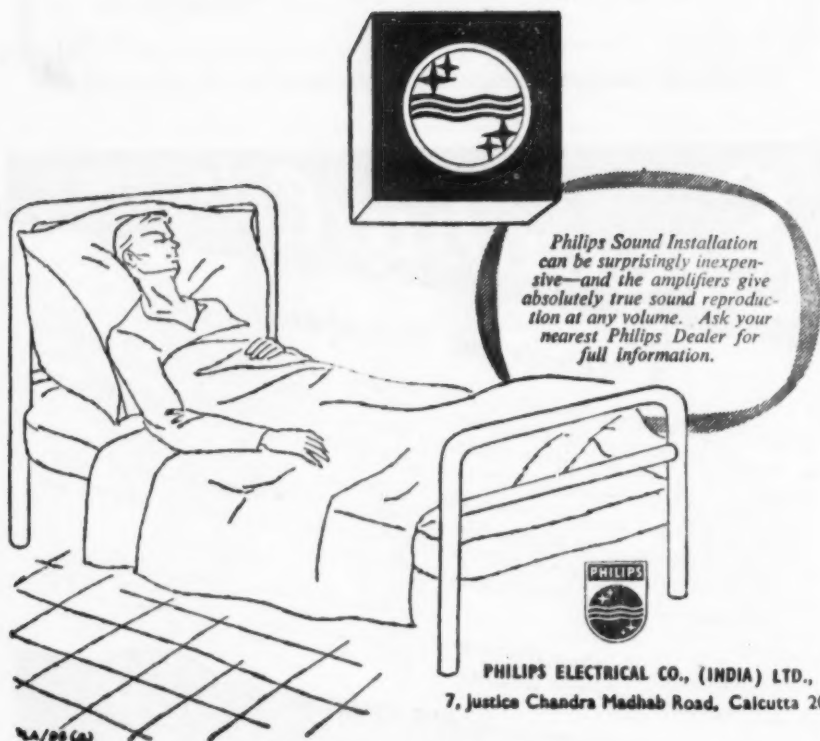


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Every doctor will agree that the physical recovery of a patient is accelerated if the mind is kept occupied and diverted from brooding. This is called Diversional Therapy and should not be too tiring. Music and radio programmes broadcast through amplifiers provide the perfect answer—the mind of the convalescent can be occupied for many hours without excessive concentration.

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*Amplifying Equipment*



The illustration shows a man lying in a hospital bed, looking relaxed. Above him is a square speaker unit with a circular logo featuring a stylized sun and waves. A speech bubble from the speaker contains text about the sound installation. In the bottom right corner, there is a Philips shield logo and the company name and address.

Philips Sound Installation can be surprisingly inexpensive—and the amplifiers give absolutely true sound reproduction at any volume. Ask your nearest Philips Dealer for full information.

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RA/95 (A)



**Thrombophlebitis**

**Leg ulcers**

**Inflammatory  
infiltrations**

**Thrombosis**



# **HIRUDOID**

**An organic preparation  
in ointment form  
with an action analogous to  
leech therapy**

# **H**IRUDOID

**constitutes the inauguration of a new active therapy because of its peculiar properties:**

- *Rapid alleviation of pain and reduction of the inflammation*
- *No control of clotting time or prothrombin level*
- *Highly economical use*
- *Simple administration*

#### **Composition:**

Substances extracted from animal organs, anticoagulant and hyperaemic in their effect, akin in their anti-thrombin action to the body's own heparin, which are absorbed by the skin, in a particularly suitable cream base

#### **Indications:**

**Localized inflammatory processes, such as**

- *Inflammatory infiltrations*
- *Thrombophlebitis*
- *Inflammation of varices*
- *Abscesses, furuncles*
- *Leg ulcers*
- *Panaricia*

**Treatment of thromboses adjacent to the surface**

**Haematoma**

#### **Packing and Application:**

Single tube of cream containing approx. 12 g. Single tube of cream containing approx. 36 g. Hospital packing containing approx. 144 g.

*The ointment is made to enter into the skin by slight friction.*

**LUITPOLD - W E R K M U N I C H**

Samples and literature available on request

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**NEW ADDRESS:-**

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**Based on the  
latest  
developments  
in HAEMATOLOGY**



A most modern anti-anaemic preparation for the treatment of diverse types of anaemias, including macrocytic and microcytic. Livules owe their efficacy to their ability to supply all the factors concerned in the regeneration of the blood.



**COMPOSITION**

Each capsule of Livules contains :—

Proteolysed Liver Powder  
Proteolysed Stomach Powder  
Ferrous Sulphate Exc.  
Thiamine Hydrochloride (B<sub>1</sub>)  
Riboflavin (B<sub>2</sub>)  
Pyridoxine Hydrochloride (B<sub>6</sub>)  
Calcium Pantothenate  
Niacinamide  
Ascorbic Acid (C)  
Folic Acid

Vitamin B<sub>12</sub>

from 50 grs. of fresh Liver.  
from 15 grs. of fresh Stomach.  
1.5 grs.  
5 mgms.  
2 mgms.  
0.5 mgm.  
1 mgm.  
15 mgms.  
30 mgms.  
1.5 mgms.  
(Livules & Folic Acid)  
5 mcgs.  
(Livules & B<sub>12</sub>)

*Livules & Folic Acid & B<sub>12</sub>,  
& Livules without Iron are  
also available.*

**LIVULES**



**ALEMBIC CHEMICAL WORKS CO. LTD., BARODA 3.**

# AMPHEDRIN

*Tablets*

In the management of

**ASTHMA**  
*AND*  
**HAY FEVER**

**Composition :**

Aminophylline	... 1½ grs.
Phenobarbital	... 1/6 gr.
Ephedrine Hcl.	... 3/8 gr.

*Prepared by*

**BIOLOGICAL RESEARCH LABORATORIES,  
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**AND**

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(WITH FOLIC ACID)

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RENOWNED PRODUCT

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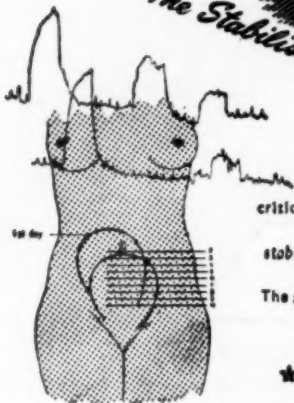
All types of Tropical Anæmia,  
Nutritional setbacks, debility  
& convalescence after prolonged illness

*For particulars please apply to :*

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*The Stabilised Ergot preparation*



Ergot therapy is called for at critical moments. The ergot preparation must be carefully standardized and stable in tropical climate. **ERGOSEAL** fills these requirements admirably. The sealed gelatin capsule packing leads to additional stability in hot and humid weather.

★ **ERGOSEAL** contains the total alkaloids of Ergot.

**HIND CHEMICALS LTD.**  
KANPUR.



To Normalise **MENSTRUAL ABNORMALITIES**

OF VARIOUS KINDS FROM  
FUNCTIONAL & GLANDULAR  
DISORDERS

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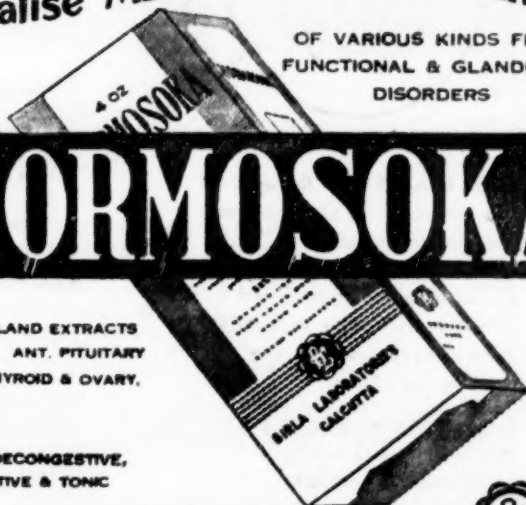
# HORMOSOKA

Contains  
**ASOKA**

**PERFECT  
CYCLE**

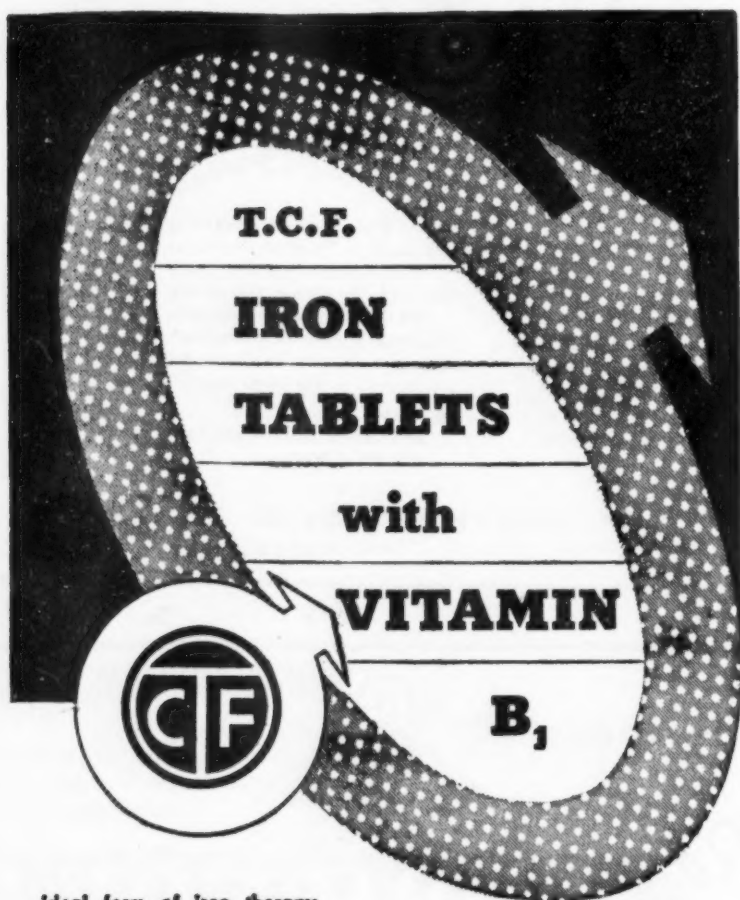
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OF ANT. PITUITARY  
THYROID & OVARY.

VEGETABLE LAXATIVE, DECONGESTIVE,  
ANTISPASMODIC, SEDATIVE & TONIC



**BIRLA LABORATORIES CALCUTTA**





**Ideal form of Iron therapy.**  
The minute traces of copper and manganese contained in T.C.F. Iron Tablets with Vitamin B<sub>1</sub>, act as catalytic agents, and render the iron fully assimilable. Vitamin B<sub>1</sub> counteracts any constipating action.

*In bottles of 50, 100 and 500 tablets; also tins of 1000 and 5000 tablets.*

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*Ample supplies available*  
**ORDER NOW!**



**PENICILLIN LOZENGES A & H.** Each contain 1,000 units of penicillin B.P. ; tubes of 20 lozenges.

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**PENICILLIN NONAD TULLE.** Emulsifying base contains 1,000 units of penicillin per gramme, tins containing 10 pieces each 4 ins.  $\times$  4 ins., and strips of 4 ins.  $\times$  2 yds.

## **A & H PENICILLIN PREPARATIONS**

**ALLEN & HANBURY'S LTD**  
(INCORPORATED IN ENGLAND)  
**CALCUTTA BOMBAY**

- ★ In Diarrhoea
- ★ Nausea & Vomiting of Pregnancy
- ★ Cases of Gastrointestinal Toxicity

## Resion

Polyamine Methylene Resin for cases  
of Gastrointestinal Toxicity

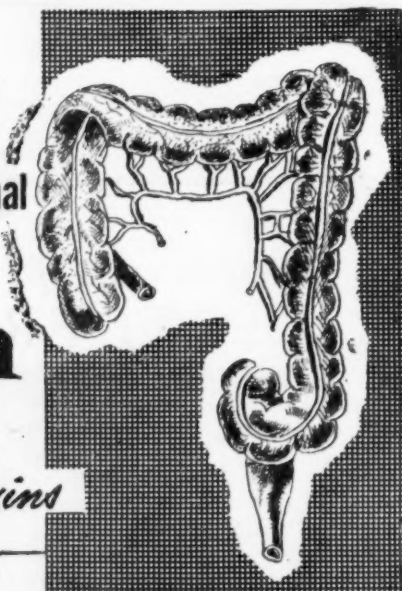
*Removes Intestinal Toxins*



THE NATIONAL DRUG CO.  
Philadelphia U.S.A.

Sole Agents in India:

C. AGRAWAL & CO. LTD. 43, Laxmi Bldg., Sir, P. M. Rd. BOMBAY I.



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"Take  twice a day"

Wincarnis has proved extremely beneficial as a tonic after illness. It is a digestive acceptable to the weakest stomach, and palatable enough for the most reluctant appetite. Wincarnis acts as a gentle stimulant which helps the patient to renewed vitality and the more active mental condition so important in recovery.

★ Wincarnis is a blend of pure, matured red wines, strengthening elements and malt extract.

## WINCARNIS

over 25,000 recommendations  
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#### ISONINDON

Isonicotinylhydrazine  
Isonicotinic Acid Hydrazide  
50 mgs. per tablet.

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Isonicotinic Acid Hydrazide 8 mgs.  
P.A.S. CALCIUM 333 mgs. per tablet.

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Pure Para-Amino Salicylic Acid  
(P.A.S.) 5 grs. per tablet.



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for  
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and  
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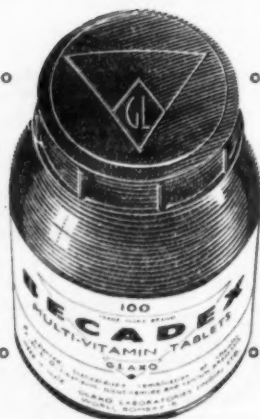


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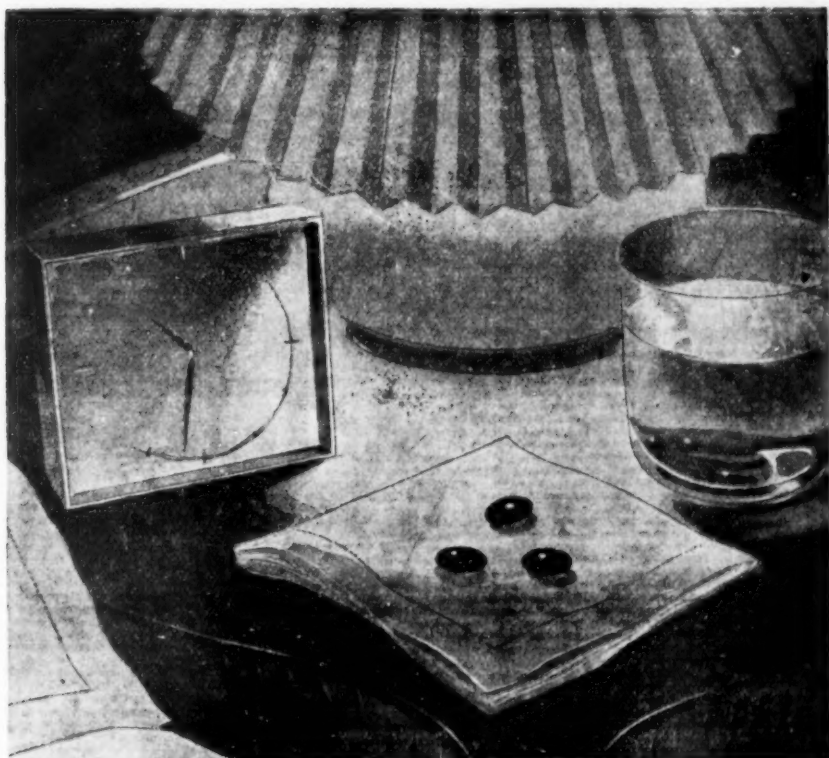
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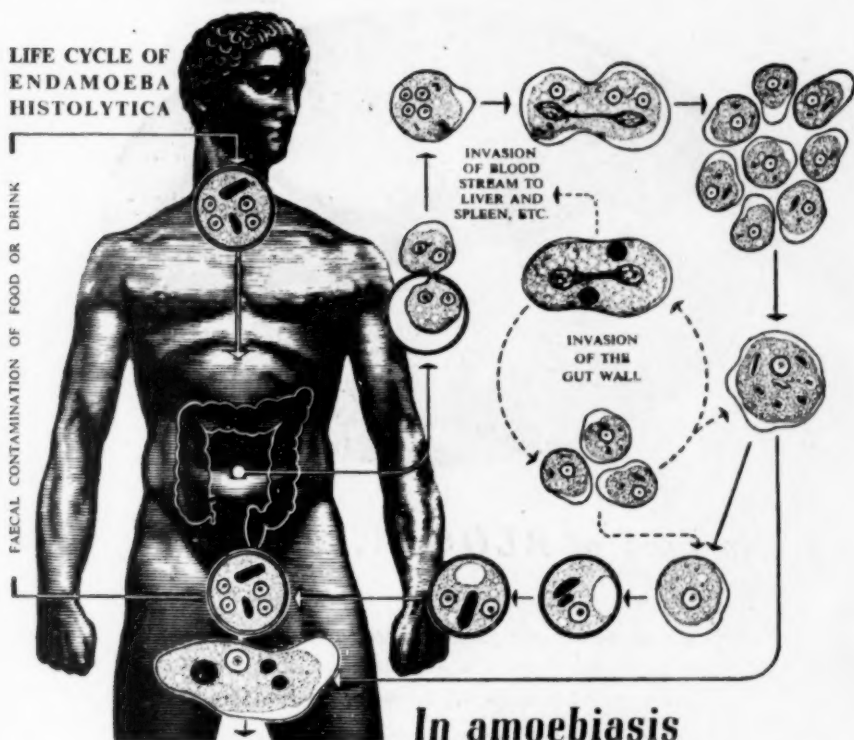


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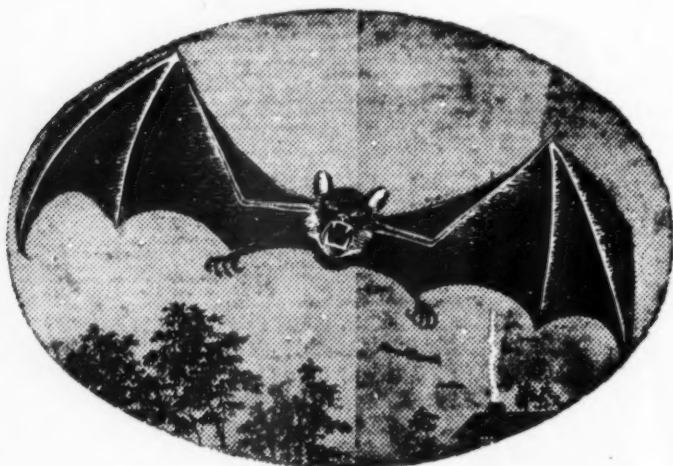
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## Original Articles

### CRYSTALLINE PENICILLIN IN MACROCYTIC ANÆMIA\*

P. L. DESHMUKH, M.D., D.T.M. & H., F.C.P.S.,

Hon. Physician, Sassoon Hospitals, Poona.

**F**AVOURABLE therapeutic results of crystalline penicillin therapy in megaloblastic anæmia have recently been reported in literature. Three cases of macrocytic anæmia treated with crystalline penicillin in the Sassoon Hospitals, under my professional care, are reported below:—

Case I.—C. S., a prisoner aged 46, was admitted on 18-10-'51 for anæmia and general weakness of six months' duration. He was unable to do any strenuous work. The patient appeared well-built but pale and weak. The liver was enlarged one finger and the spleen two fingers. The lungs appeared clear on physical examination and fluoroscopy. The urine and stool were normal. Gastric analysis showed histamine-fast achlorhydria, with low total acidity. Kahn test of the blood was negative. Reports on his blood on different occasions were as follows:—

	31-8-'51	1-10-'51	18-10-'51	8-11-'51
R.B.C.	... 1'35 mill.	1'64	2'44	2'76
W.B.C.	... 2200	2250	4850	5600
Hb.	... 6 g.	5'5 g.	9 g.	12'5 g.
P.C.V.	... 17 p.c.	16 p.c.	31 p.c.	32 p.c.
M.V.V.	... 126 c. y	151	122	115
M.C.H.	... 44'4 yy	52'9	36'9	41'6
M.C.H.C.	... 35'3 p.c.	34'3 p.c.	29 p.c.	39 p.c.
E.S.R.	... 50 mm.	72	18	49

(Wintrobe 1 hour.)

\* Specially contributed to THE ANTISEPTIC.

Other examinations on 31-8-'51 showed :—Total blood proteins 5.6% with the Alb : Glob ratio. as 3.98 : 1.62. Icterus index 7. Sternal marrow examination on 4-10-'51 showed a megaloblastic reaction.

**TREATMENT :—**The treatment given before and between the blood check-ups was as follows :—

18-8-'51 to 31-8-'51 :—Iron mixture daily, one injection of liver extract 2 cc. Fersolates one t.d.s.

1-9-'51 to 1-10-'51 :—Acid hydrochlor mixture daily, 8 injections of liver extract 2 c.c. each. Fersolates one t.d.s.

2-10-'51 to 18-10-'51 :—Mixture and tablets continued as before. Inj. crystalline penicillin, 2 lac units twice a day, for 7 consecutive days 2nd to 8th October, making a total dose of 28 lacs.

18-10-'51 to 8-11-'51 :—Mixture alone continued as before. Inj. crystalline penicillin 2 lac units per day for 10 consecutive days (from 26-10-'51 to 5-11-'51) making a total dose of 40 lac units.

The patient was discharged on 16-11-'51 in a greatly improved condition.

*Comment :—*The blood reports on 31st August and 1st October showed that there was no response to iron and acid mixture orally and to injections of liver extract. A remarkable change in the blood condition was noted in the next two blood reports on 18th October and 8th November respectively, the former after 28 lacs and the latter after another 40 lac units of crystalline penicillin parenterally. It will be noted that : (1) Hb. increased first by 63% and after the second course of penicillin to 127% over the original level. (2) R.B.C. count increased by 50% and then by a total of 69%. (3) W.B.C. count increased by 118% and 154%. (4) P.C.V. increased by 93% and 100%. (5) There was a tendency to a diminution in the size of the R.B.C.

The E.S.R. appeared to have varied with M.C.H. Improvement in the blood condition was marked after the first course of penicillin, and less so after the second.

Case II.—B.G.M., a farmer, aged 50, was admitted on 24-10-'51 with complaints of weakness, loss of appetite and swelling of feet, of three months' duration. The liver and spleen were not palpable. Urine was normal. Cysts of *Ent. histolytica* were found in the stool. The lungs appeared normal on physical examination and fluoroscopy. Gastric analysis showed the total and free-acidity to be within normal limits. Kahn test of blood was negative. Reports on blood on different occasions showed :—

	2-11-'51	19-11-'51	30-11-'51
R.B.C.	.. 1'68 mill	1'84	2'4
W.B.C.	.. 5700	4500	2200
Hb.	.. 6'5 g.	9 g.	10 g.
P.C.V.	.. 19 p. c.	28	31
M.C.V.	.. 113 c. y	152	129
M.C.H.	.. 38'7 y y	48'9	41'6
M.C.H.C.	.. 34'2 p. c.	32'2 p. c.	32'2 p. c.
E.S.R.	.. 42	61	45

(Wintrobe 1 hour.)

TREATMENT:—24-10-'51 to 2-11-'51:—Enterovioform tablets, one t.d.s. Iron mixture.

3-11-'51 to 19-11-'51:—Alkaline mixture. Injection of crystalline penicillin 2 lac units twice a day for 8 consecutive days, from 9th to 16th Nov. '51 making a total dose of 32 lac units.

20-11-'51 to 30-11-'51:—Alkaline mixture. Inj. of crystalline penicillin 2 lac units twice a day, for five days from 25th to 29th Nov. '51, making a total of 20 lac units.

The patient was discharged on 11-12-'51 in a greatly improved condition.

*Comment*:—This patient had macrocytic anaemia with normal gastric acidity. For his latent amebic infection he received Enterovioform tablets, the administration of which, in our opinion does not vitiate the results of penicillin therapy to any appreciable extent. The response to the two courses of crystalline penicillin with 32 and 20 lac units respectively may be summarized as follows:—

(1) R.B.C. count increased by 12% after the first course, and 50% after both the courses. (2) W.B.C. count was diminished by 22% and 62%. (3) Hb. increased by 38% and 54%. (4) P.C.V. increased by 47% and 63%. (5) M.C.V. first increased and then diminished.

The E.S.R. increased after the first course indicating that the action of penicillin on blood regeneration was not due to the control of a septic focus. If it were so, one would expect a reduction rather than an increase in E.S.R. The E.S.R. appeared to vary roughly with the M.C.V. and M.C.H.

The response to the first course was more marked than to the second.

Case III.—M.V.D., a goldsmith, aged 25, was admitted on 22-8-'51 for general debility and anaemia of two months' duration. Physical examination did not reveal anything particular except the anaemia. The liver and spleen were not palpable. He ran an irregular temperature on admission which promptly responded to antimalarial treatment. The urine was normal, but the stool showed ascaris infection. Gastric analysis revealed histamine-fast

achlorhydria. The lungs were clear on fluoroscopy. The Kahn test of the blood was negative. The examination of his blood on different occasions revealed:—

	31-8-'51	18-9-'51	28-9-'51	16-10-'51
R.B.C.	.. 0.78 mil.	0.6	1.0	1.16
W.B.C.	.. 3100	3500	2300	4400
Hb.	.. 3 g.	2 g.	2.5 g.	3.5 g.
P.V.C.	.. 12 p. c.	8.5	9	13
M.C.V.	.. 154 c. y	141	90	118
M.C.H.	.. 38.4 yy	33.3	25	31
M.C.H.C.	.. 25 p. c.	23.5 p. c.	27.8 p. c.	26
E.S.R.	.. 75 mm.	—	70	70
Proteins	.. 5.4	8	—	—
Serum Alb.	.. 3.32	4.64		
Serum Glob.	.. 2.08	3.35		

8-10-'51:—Reticulosis was 1% and the bone marrow examination showed megaloblastic reaction.

TREATMENT:—22-8-'51 to 30-8-'51:—Santonine. Iron mixture three times a day.

31-8-'51 to 18-9-'51:—Santonine. Acid mixture. Six injections of Uniferron intravenously making a total dose of 540 mg. of iron. Two injections of Quinine dihydrochlor 6 gr. each. 7 days Mepacrine tablets, one t.d.s. Blood transfusion, 250 c.c. 18-9-'51.

19-9-'51 to 28-9-'51:—Acid mixture. Fersolates one t.d.s. Two injections of liver extract of 2 c.c. each.

29-9-'51 to 16-10-'51:—Inj. crystalline penicillin two lac units b.d. for 9 days (30th Sept. to 8th Oct.) making a total dose of 36 lac units. Blood transfusion 100 c.c. on 16-10-'51 (more blood was not given as the patient had a severe reaction after the 100 c.c.)

16-10-'51 to 21-11-'51:—Inj. B<sub>12</sub> and Folic acid. Blood transfusion.

The patient showed rapid improvement after 16-10-'51 and he was discharged 21-11-'51 in a greatly improved condition.

*Comment:*—This patient gave a weak response to crystalline penicillin therapy, while his response to B<sub>12</sub> and Folic acid was prompt and satisfactory. The significant blood changes that were observed in the response were: (1) A rise in Hb. 40%; (2) 10% rise in R.B.C. count; (3) 94% rise in W.B.C. count; (4) P.C.V. increased by 44%; (5) M.C.V. increased by 31%. The reason why response to penicillin was so weak could not be determined.

*Discussion.*—The cases described are undoubtedly cases of macrocytic anemia—Cases Nos. 1 and 3 may be called megaloblastic owing to megaloblastic reaction of the bone marrow. In Case No. 2, the bone marrow was not examined. In no case were megaloblasts or even nucleated R.B.Cs. found in the peripheral blood.

Cases Nos. 1 and 3 showed histamine-fast achlorhydria, while Case No. 2 showed normal gastric acidity. The response of all the three cases to crystalline penicillin as judged by the rise of Hb. content and R.B.C. count suggests that crystalline penicillin probably possesses a stimulating action on the hæmopoietic system comparable to that of B<sub>12</sub>, Folic Acid or liver extracts. The response appears to be irrespective of the presence or absence of free hydrochloric acid in the gastric secretion. Age and sex do not seem to influence the response. In the above cases, age has varied from 25 to 50 years. Though all our three cases were males, two cases of females are described by Foy *et al.* The probable aetiological factors in our three cases were:—malaria in Case No. 1, amœbic infection in Case No. 2, and ascariasis *cum* malarial infection in Case No. 3.

As regards the nature of response, (*see Table*) it is seen that R.B.C. count, W.B.C. count, Hb. content and P.C.V. have tended to rise in all cases. The rise in Hb. and W.B.C. count appears to be the most spectacular. It was remarkable that where the injection of liver extract in Case 1 and of intravenous iron in Case 3, failed to produce a response, crystalline penicillin succeeded.

The following table shows the important changes in the blood picture in response to Crystalline Penicillin therapy.

Percentage rise (+) or fall (–) in

	Cryst. penicillin in lacs.	R.B.C.	W.B.C.	Hb.	P.C.V.	M.C.V.
Case I	28	+ 50	+ 118	+ 63	+ 93	– 20
	68	+ 69	+ 154	+ 127	+ 100	– 24
Case II	32	+ 12	+ 22	+ 38	+ 47	+ 36
	52	+ 50	+ 62	+ 54	+ 63	+ 17
Case III	36	+ 10	+ 94	+ 40	+ 44	+ 31

It is worth remembering that penicillin in large doses is found to be valuable in the treatment of agranulocytosis, where it is found to increase the number of circulating granulocytes and also improve the general blood-picture. The response obtained in the cases described above, does not appear to be dissimilar to that obtained in agranulocytosis.

From the data available at present, it is difficult to explain the favourable action of crystalline penicillin in these cases of anæmia. The following are suggested as the probable modes of action:—

1. Crystalline penicillin probably contains a hæmopoietic principle resembling B<sub>12</sub> or Folic acid, as there is a marked similarity in the two responses.

2. Crystalline penicillin may favourably influence a septic or toxic process and thus diminish or remove any depressant action on the hæmopoietic tissue arising therefrom. No toxic or septic focus was detected in the cases described except the infections mentioned.

The rise in W.B.C. count in all cases and the changes in E.S.R. do not support the view.

3. Crystalline penicillin may induce a change in the intestinal bacterial flora and bring about (a) a better absorption of the hæmopoietic principle, (b) an improved bio-synthesis or activation of the missing hæmopoietic principle or (c) an eradication of the factors that destroy the hæmopoietic principles or prevent its absorption or action. At present, this is in the nature of pure speculation. An extended micro-biological investigation would be necessary to confirm or negative the possibilities indicated above.

We do not wish to enter into a discussion on the various aspects of megalocytic, megaloblastic and pernicious anæmias, as we are here mainly concerned, with the reporting of the hæmopoietic response (of this group of anæmias) to crystalline penicillin.

Conclusion.—No conclusions of value can be drawn from the meagre clinical data presented. But the finding that parenteral crystalline penicillin was found to influence favourably the macrocytic anæmia in the cases reported, is inescapable. Gastric acidity appeared to play no part in influencing the response. The mode of action of crystalline penicillin in these anæmias, though undetermined as yet, appears to be similar to that of other hæmopoietic principles like B<sub>12</sub>, Folic acid and crude liver extract. Crystalline penicillin therefore, deserves a trial in case of obstinate macrocytic anæmias.

Summary.—Three cases of macrocytic anæmia (two of them with megaloblastic reaction in the bone marrow), treated primarily with parenteral crystalline penicillin are described. Two of them had histamine fast achlorhydria. The response was quite satisfactory in the first two cases but less so in the third. The probable role of crystalline penicillin in favourably influencing macrocytic anæmias is discussed.

#### References

1. Foy *et al.*, (1951), Br. Med. Jour., 24 Feb. p. 380.
3. Foy *et al.*, (1951), Br. Med. Jour., 19 May, p. 1108.

### Life Span of Eos/nophilic Granulocytes

When eosinopaenia is produced by administration of corticotrophin to persons with marked blood eosinophilia, it can be observed that eosinopaenia occurs again after a definite interval. This is apparently due to a destruction of the cells that have been formed in increased numbers during the regenerative phase and the phenomenon is therefore, designated as an "equalizing eosinopaenia". A method for determination of the life-span of granulocytes is based on this phenomenon. Studies carried on by the authors suggest that the total life span of the eosinophils is about six days whereas the life span of the circulating eosinophils is only about 2 days.—(*Schw. Med. Wchns.*, 828: Abst. in *J.A.M.A.*, 150: 4, 1952).

## AN INTRODUCTION TO THE NORMAL BLOOD PRESSURE IN BEHARIS\*

B. B. DOTTO,

*Chief Medical Officer of the Police Co-operative  
Life Insurance Society, Limited, Calcutta-13*

My article in the *ANTISEPTIC* for January, 1952, on the minimum, average and maximum blood pressure in Indians was reprinted or extracted in some of the leading Insurance Journals and periodicals in India and several medical examiners and life assurance companies have since requested me to record my observations on the blood-pressure in Beharis, who are taking life assurance protection in greater numbers than ever before. I had given the mean of the systolic, diastolic and pulse pressure in 3,000 Beharis, in the last article mentioned above.

During the last fourteen years, I have made four investigations on the average blood pressures in Beharis. The first one was in 1948 on 875 persons, the second in 1949 was on 1,750 lives, and third in 1950 on 3,000 entrants and the present one, the fourth, in 1952, relates to 5,000 subjects. I am not aware of any previous investigation on the average blood-pressure in Beharis. In 1942, Col. Chopra, published the mean of systolic, diastolic and pulse pressures in Bengalees, Beharis and Oriyas combined together, based on 3,522 recordings.

The present investigation covers the period from 1947 to 1952, (inclusive). All the entrants are employees in the West Bengal and Calcutta Police Forces and in the West Bengal Fire Services—who proposed to insure their lives with the Police Co-operative Life Insurance Society, Ltd. The total number is thus fully representative as it comprises Inspectors, Sub-inspectors, subedars, jama-dars, havildars, assistant sub-inspectors, head-constables, lance naiks, sepoy, constables, drivers, orderlies, leading firemen, fire engine drivers, cleaners, carpenters, mechanics, etc.

Out of the total of 5,000 Behari subjects included in this investigation, 1,442 or 28·84% were single, and 1,656 or 33·12% were vegetarians; 4,260 or 85·2% were Hindus and the remaining 740 or 14·8% were Muslims; 4,855 or 97·1% smoked or took tobacco in some form or other and 472 or 9·44% took alcoholic drinks regularly or on festive occasions only.

Many proposals were received from the mofussil. As medical reports from outstations were in many cases unreliable, experienced medical examiners were deputed from Calcutta to mofussil stations to examine the proposers, so as to maintain a high standard of examination; 3,174 or 63·48% of the applicants were examined in Calcutta.

\* An abridged version of this paper under the caption "Short Notes on the Normal Blood Pressure at Beharis" was read in the Bihar Insurance Conference, held at Patna on the 28th March, 1953, under the auspices of the Patna Insurance Club.

I have personally recorded the blood pressure in 3,072 cases or 61.47% of the total entrants, who were examined in my presence. I used the latest life-time Baumanometers (Wall-type, 300 mm. and Kompak model) manufactured by Messrs. W. A. Baum Co. Inc. of New York. The other examiners also used Baumanometers exclusively in order to ensure uniformity of readings. In 1950, the manufacturers sent me an "Air-Lok" cuff which has been used by me ever since.

The "Air-Lok" cuff embraces several improvements over the old types of arm-bands, is very simple to use and has now become a standard equipment on all Baumanometers. In March 1952, the manufacturers sent me for trial and opinion a "Sani-Genic" cuff, which was then still in the experimental stage. I used this in over 2,000 readings with great ease and satisfaction. This new cuff is more hygienic and made of inextensible plastic-coated fabric, impervious to perspiration, easily wiped clean or washed with soap and water; it can be even sterilized if and when required. It is thus best suited for use in tropical countries. It is perhaps the first cuff containing a built-in inflation bag. The cuff retains the fully conforming "wrapped" cuff principle and is effectively restrained from slipping or "ballooning" by its high friction surface and reserve-wrap. The greater the applied pressure, the tighter it holds. In March 1953, the same manufacturers sent me two of their "new cleanable "Air-lok cuff"—which is the new trade-name for the "Sani-Genic" cuff. These new cuffs have recently been placed on the American market and may become available in India in the near future. "The new cleanable Air-lok cuff" will, it is claimed, revolutionize the blood pressure recording technique and it may be used with any make of sphygmomanometer.

Following my usual practice, the blood pressures were recorded at least two hours after the meal and after making sure that the subject was not under the influence of alcohol or tobacco at the time of the examination. The auscultatory method alone was used and more than two additional readings were taken in cases of doubt or abnormality. In a small number of subjects the palpatory method was adopted as the arterial sounds were not distinctly audible. Nervous individuals—who formed less than 10% of the total entrants—were re-examined, 3 to 7 days after the initial examination to eliminate the effects of nervousness and this yielded satisfactory results. In extremely nervous individuals it was found that the systolic pressure increased by 30 to 40 mm. in the first one or two recordings, and settled down to normal when a fresh reading was taken after a few days' interval. Nervousness has only a slight effect on diastolic pressure, not over 10%. This has been noticed in a very large number of recordings.

In the present investigation the average systolic, diastolic and pulse pressures in Beharis were found to be 122.8, 79.1 and 43.7 mm.

Hg. respectively (*vide* Table on page 634). In the first investigation the average systolic, diastolic and pulse pressures in Beharis were 121·8, 79·2 and 42·6 mm. Hg. respectively. In the second investigation the average systolic, diastolic and pulse pressures in Beharis were 121·5, 78·3 and 43·2 mm. Hg. respectively. In the third investigation the average systolic, diastolic and pulse pressures in Beharis were 120·0, 79·2 and 42·8 mm. Hg. respectively.

It may be stated that in the 1949 investigation on 5,000 Indians (inclusive of 1,750 Beharis) the average systolic, diastolic and pulse pressures were 122·8, 79·3 and 43·5 mm. Hg. respectively. In an earlier investigation relating to 2,500 Indians (inclusive of 875 Beharis) the average systolic, diastolic and pulse pressures were 123·4, 80·2 and 43·2 mm. Hg. respectively. In the latest investigation of 1950 comprising 10,000 Indians (inclusive of 3,000 Beharis) the average systolic, diastolic, and pulse pressures were 122·6, 79·6 and 43·0 mm. Hg. respectively. In an investigation comprising 3,000 Indian females (inclusive of 223 Beharis) made in 1950, I found the average systolic, diastolic and pulse pressures in Indian females to be 118·5, 78·0 and 40·5 mm. Hg. respectively. In a still earlier investigation made in 1947 with 1,674 entrants I found the average systolic, diastolic and pulse pressures in Indian females to be 119·2, 78·2 and 41·0 mm. Hg. respectively.

From the above, it will be seen that the average systolic, diastolic and pulse pressures in Behari subjects are the same as those for Indians in other States. Col. Chopra however, found the average systolic, diastolic and pulse pressures in Bengalis, Beharis and Oriyas combined, to be 114·7, 76·2 and 38·5 mm. Hg. respectively. These figures are remarkably low. In my previous articles, I had recorded that the inclusion of blood pressures (1) of 1,895 females, (2) of youngsters, and (3) of hospital patients, probably accounted for the low mean figures obtained by him and he did not specify the number of entrants in each age-group. His figures are not followed by our life assurance companies or medical examiners. They were following the blood pressure table based on 1372 readings prepared by the Oriental Life Assurance Company nearly three decades ago. The blood-pressure-tables formulated by me in 1952, based on 10,000 readings, have been accepted as the popular standards for India and are being extensively used by all the progressive life assurance companies and medical examiners. My blood pressure and height and weight tables have been published in the Indian Insurance Directory, Insurance Vade-Mecum, Sodhi's Insurance Red Book, etc.

I shall be failing in my duty if I do not express my grateful thanks and sense of indebtedness to Mr. S. N. Chatterjee, B.A., I.P., J.P., Chairman of the Society for kindly according permission to me to publish the results of this investigation.

Table showing Average Arterial Pressure in 5,000 Behari Personnel of the West Bengal and Calcutta Police Forces and West Bengal Fire Services.

Age group years	Number of entrants	Average systolic pressure	Average diastolic pressure	Average pulse pressure
18-19	1,060	114.6	74.0	40.6
20-24	1,080	116.8	75.2	41.6
25-29	1,298	118.0	76.0	42.0
30-34	558	121.9	78.4	43.5
35-39	430	124.7	80.6	44.1
40-44	234	126.5	81.5	45.0
45-49	216	128.8	83.2	45.6
50	124	130.6	84.5	46.1
Total entrants.	5,000			

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### Long-term Results with Corticotrophin and Cortisone

The Danish Medical Press is now publishing long term results reflecting the experiences of several years. Drs. Bratlund and Holten of the Aarhus University Hospital report their experiences with 40 patients suffering from rheumatoid arthritis and treated between 1.3.1950 and 31.8.1952. During the same period 126 others with rheumatoid arthritis were not given cortisone or corticotrophin though they were treated in the same hospital. Cortisone was given by mouth at first in large doses and later in comparatively small doses for maintenance. In 33 cases good results were reported. While in the other 7 the results were not satisfactory. 29 of the 40 were able to resume work on discharge from hospital and 26 of these are still at work. Dr. Fischer and Prof. Brochner-Mortensen of the Rigshospital Copenhagen, treated 51 patients with chronic polyarthritis between June 1949 and January 1953. In 37 of these the response was favourable in 8 the improvement was less pronounced and in 6 there was either no change or the patient got worse. The number of completely disabled patients was reduced from 11 to 4. Though this treatment gave rise to no dangerous or fatal complications, side effects were observed in nearly every case.

In a leading article in *Ugeskrift for Læger* (5.2.53), the position with regard to these two hormonal products is very well reviewed. They have not proved of any value in arthrosis, and rheumatic fever may not respond more effectively to the two drugs than to large doses of salicylates. They have shown themselves remarkably effective in Addison's disease, status asthmaticus, and various diseases of the eyes, skin and vascular system.—(Letter from Denmark in *J.A.M.A.*, 23.5.1953, p. 352).

## THE TREATMENT OF RELAPSING FEVER WITH ANTIBIOTICS\*

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"IT is often a matter for anxious consideration whether the patient's chances of recovery are better with or without the drug; in mild cases in young patients the disease is not a threat to life, in severe cases the drug is more likely to be risky."

The drug is Neoarsphenamin given intravenously and the author of this statement is Sir Leonard Rogers in his standard book "Tropical Medicine" in the chapter dealing with the specific treatment of relapsing fever. The supreme demand for any modern treatment of diseases is its harmlessness for the patient. Any treatment which carries risk to life must be discarded.

Relapsing fever occurs in epidemic form in Ethiopia and its classical treatment with Neoarsphenamin often caused us the same anxiety as that which Sir Rogers predicted about the patient's chances of recovery and we actually lost patients by its administration on account of circulatory shock. That is why we felt the urgent need for a safe drug with the same or possibly even greater curative properties. We have since found that the antibiotics Chloromycetin and then crystalline penicillin fulfil these demands.

We find in the literature, only two papers dealing with antibiotics in relation to relapsing fever.

Berks and Goodwin reported that Terramycin had a potent effect on *Spiroplasma duttoni* in mice. Single doses of 200 mg. of terramycin per kg. by mouth prevented death of heavily infected mice during the initial parasitemia but did not prevent relapse. Five daily doses of 200 mg. per kg. effected a cure, no spiroplasmata being observed in the blood during a period of six weeks.

Harrison and Whittington found six of seven patients with louse-relapsing-fever responding well to treatment with 200,000 units of aqueous penicillin every six hours for ten-days. Another patient who was given 300,000 units of procaine penicillin twice a day, for 24 hours became afebrile and his blood-smear negative for *Borrelia*. But two days later, the authors had to repeat the above treatment with aqueous penicillin. The patient continued afebrile for a full three-weeks period. A single patient was treated with aureomycin and showed almost as good results as with aqueous penicillin.

Chloromycetin.—The makers of Chloromycetin claim that it shows remarkable activity *in vitro* against a strain of *Borrelia recurrentis* against which concentrations of 100 units per cc. of penicillin were inactive. There exists, however, no published record on the effect of Chloromycetin on men suffering from fever recurrentis.

\* Specially contributed to THE ANTISEPTIC.

We, therefore, decided to try chloromycetin in the treatment of this disease. Because of its being suitable for oral administration we considered that, as a curative, it may have a less drastic effect on the patient than neoarsphenamin and so it may prove to be the drug we were looking for. We have now used this new line of treatment on more than 200 patients and found it superior in every respect to neoarsphenamin; we have not lost a single patient, the remission is prompt and not followed by complications of any sort, there is no Herxheimer reaction, no circulatory collapse, there is clinically no recurrence of fever and no reappearance of the spirochætæ in blood-smears during the follow-up periods of between one and two months. We believe, however, that even later no relapse occurs since every patient is asked on discharge to report and get himself re-admitted in case of renewed fever. Since this is the only hospital for the whole district the patients have nowhere else to go and so relapses if any, should necessarily come to our notice. This is supported by the fact that patients who had previously been treated with neoarsphenamin by us and who got subsequent relapses always returned to us for treatment.

We give as a rule a total dose of 3 g. by mouth (twelve capsules of 250 mg. each) in divided doses of 500 mg. (two capsules of 250 mg. each) every six hours. This dose is adequate to render the patients afebrile, and the blood-smears negative and also to prevent relapses. Patients are usually afebrile within 24 to 48 hours, the drop in temperature occurring by lysis and not by crisis. The patient's recovery is usually rapid and uneventful. None of the dangerous signs previously encountered in neoarsphenamin therapy, such as heart-failure, Herxheimer reaction or temporary mental derangement were experienced with chloromycetin.

Every one of our 200 patients and more under review was, of course, diagnosed by blood-smears and/or thick drops stained with Giemsa's stain before starting chloromycetin treatment. However, in places with no laboratory facilities, the differential diagnosis of relapsing fever is difficult, since the clinical picture of relapsing fever resembles, besides other diseases, that of typhus and typhoid. It is under such field conditions that chloromycetin offers an additional advantage as a curative for these diseases.

Aureomycin and terramycin.—These antibiotics have been used by us on a small number of patients suffering from relapsing fever. They are apparently of about equal effectiveness and harmlessness as chloromycetin; we administer them in the same way as chloromycetin. These findings however, require confirmation by further clinical investigations.

Crystalline penicillin.—The high cost of the group of antibiotics mentioned *supra* is a prohibitive factor when hundreds of cases of relapsing fever have to be treated. For mass-treatment a

cheaper and effective substitute will be required. Obviously, the antibiotic of choice is crystalline penicillin soluble in water which is cheap and has proved its value in the treatment of syphilis, the causal organism of which resembles that of relapsing fever. In order to test the susceptibility of the relapsing fever spirochætæ to crystalline penicillin, we injected 50,000 units in aqueous solution to one group of four patients intravenously and to another group of four patients intramuscularly. In the intravenous group two patients became afebrile within twelve hours and the spirochætæ disappeared from the peripheral blood about one hour before the drop in temperature set in. After seven days, however, both the patients got a relapse and required another 50,000 unit-dose to get cured. The two other patients in this group did not respond satisfactorily to this dose, their fever-curve showed only a limited downward trend their blood smears were never free from spirochætæ. In the intramuscular group this dose proved inadequate in all four cases, two of them showed only slight response but never touched normal and required immediate further penicillin treatment; the two others remained entirely untouched by this dose.

Conclusions.—The following conclusions appear justifiable from these results of our preliminary investigation with cryst. penicillin in the treatment of relapsing fever:

(1) Relapsing fever is susceptible to treatment with cryst. penicillin injections.

(2) The intravenous administration of cryst. penicillin has no particular advantage over the intramuscular route. Even if smaller intravenous doses suffice to bring about the control of fever, this possible advantage does not offset the certain disadvantage due to the frequent and rather shock-like effect on the patient as a whole and particularly on his circulatory system with a suddenly decreased blood-pressure and almost imperceptible pulse when the fever drops. The patient is left in a general state of exhaustion similar to that experienced after the use of Arsphenamin.

We, therefore, resorted in our further investigations to the intramuscular route only and had now to determine the average curative dose of cryst. penicillin. Of twenty patients so treated, six were cured with one I.M. injection of 100,000 units only, seven with two injections of 200,000 each and seven with three injections of 200,000 each.

These doses effected full clinical cure, blood smears remained negative for spirochætæ and no relapse took place within one month of follow-up. The number of patients thus treated and the follow-up period are too small to permit definite conclusions to be drawn on the optimal curative dose of cryst. penicillin. We propose to report later on after making observations on a larger number of patients. But our present observations show that the curative dose

varies among patients according to the age, their general and nutritional status and according to the number and virulence of the spirochætæ. A total dose of between 400,000 and 600,000 units in divided doses of 200,000 units every 12 hours or in case of fever-relapse, is the average dose required to effect a cure. If even after this average dose, another and occasional relapse should occur, one more injection of 200,000 units will eventually cure the disease effectively.

*Comment*.—In view of the specific effective and at the same time harmlessly curative properties of the above antibiotics, the administration of the dangerous drug neoarsphenamin is no longer justifiable in the treatment of relapsing fever.

*Summary*.—In our search for a less dangerous and toxic remedy for relapsing fever than neoarsphenamin we treated more than 200 cases with chloromycetin and found it to be equally specific and at the same time absolutely safe and mild in its after-effects. No complications occurred. It prevented clinical relapses and eradicated the spirochætæ from the peripheral blood. In a small series of patients with relapsing fever the antibiotics aureomycin and terramycin were tried and found to be almost equally effective and harmless as chloromycetin.

Crystalline penicillin in aqueous solution given intramuscularly in doses between 100,000 units and 600,000 units in divided doses of 100,000 and 200,000 units each respectively, proved to be as specific and harmless as chloromycetin in the treatment of 20 cases of relapsing fever. Because of its cheapness it is the drug of choice for mass treatment.

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#### *Acute Poisoning from use of Isopropyl Alcohol in Tepid Sponging*

Rubbing alcohol is commonly used in hospitals for tepid sponging of febrile children, but little note has been made of the possible dangers inherent in the practice. A case of acute poisoning produced by tepid sponging with isopropyl alcohol, (of a 22 month old boy admitted to the pædiatric ward of St. Joseph Hospital, Kansas City) is presented by Dr. Garrison. Intoxication in this case was undoubtedly the result of inhalation and the large quantity of alcohol used in a small ill-ventilated cubicle. Sponging with cool or cold water is a more desirable method for reducing temperature than sponging with alcohol, because of this danger. The child had to be treated over a period of several hours, with caffein injections, oxygen and fluid administration, before he recovered completely after 24 hours.—(*J.A.M.A.*, 152: 4: p. 317: 1953).

# RAPID SEROLOGICAL TESTS FOR SYPHILIS\*

Principles, Technique and Interpretation of Results

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## PART I

Principles and technique of rapid serological tests for syphilis (S. T. S.)—*Antibody formation*:—When foreign matter is introduced into the body, the latter reacts to it, by producing certain antistances called '*antibodies*' and the foreign substance is called the '*antigen*'. These may be specific or non-specific or say, type-specific. This is true for both—bacterial and non-bacterial proteins. The lipoids are normally very little antigenic by themselves but when combined with proteins produce antibodies which are specific to themselves but group-specific only to proteins. These are called '*haptens*'.

The *treponema pallidum*, the causative organism of syphilis also produces certain antibodies in the patient's body. Their exact nature is not known but they are more than one in number. According to Dr. Allsande, these are anti-lipoidal, anti-treponemal thermostable, anti-treponemal thermolabile. The anti-lipoidal antibodies are probably produced by the outer layers of *T. pallidum*, which contain a fatty substance. These antibodies are similar to those produced by the injection of a fatty extract of human or ox-heart. The latter when combined with cholesterol or any other sensitiser, which forms a coating on its particles, forms an antigen which either fixes the complement or leads to precipitation, in the presence of syphilitic sera an important observation which has formed the basis of all serologic tests for syphilis.

It has been further observed that the antibodies and antigen particles when in solution are hygrophil in nature individually. But when mixed together they become hygrophobe in nature, clump together, form more compact masses and depending upon their relative weight, either settle down to the bottom of the tube or float on the surface, by producing what is known as flocculation or precipitation.

*Antigens*:—The antigens used in the serological tests for syphilis are usually non-specific in nature and consist of two components:—(1) the antigen, e.g., heart extract or cardiolipin and lecithin etc. (2) the sensitiser such as cholesterol or balsam of tolu etc., the former to determine its specificity and the latter its sensitivity. In making the test, the antigen emulsion and test sera are mixed with each

\* Specially contributed to THE ANTHROPOLOGIST.

other in definite proportions so as to conform to certain conditions and the end-product is examined for the presence or absence of agglutination.

**Selection of test technique.**—Excepting Nelson's treponemal immobilisation test, which is highly sensitive and specific—the main requisites of an ideal test, the other routine tests are more or less non-specific. Nelson's test is a very complicated one, requiring complex apparatus etc., and is therefore, unsuitable for use in the smaller laboratories in general and in the field laboratories in particular. The test technique best suited for the type of work and the facilities available will therefore, have to be chosen.

**One or more tests:**—Moore and other eminent syphilologists recommended the use of a battery of tests to be carried out as a routine, because it not only serves as a good intra-laboratory check for efficiency, but also helps to some extent in detecting biologically false positive reactions.

The WHO V. D. Demonstration Team in South East Asia, has been performing two tests and teaching their techniques. One utilises cardiolipin, lecithin and cholesterol as antigen, and is used in the Venereal Disease Research Laboratory test (VDRL test) and the other one uses heart-extract, balsam of tolu and Trypan blue and is used in Kvittingen's slide modification of Meinicke's Klearance reaction (MKLR).

Both (1) are slide-tests involving few pieces of apparatus; (2) offer a good comparison between results obtained by crude and refined antigens and those between cholesterolised and non-cholesterolised ones; (3) are easy to perform under field conditions; and (4) the MKLR test can be performed on active sera, hence most suitable for field conditions, as there is practically no necessity for the separation of sera.

**I. Individual test.**—(*Broad outlines only*).—**MKLR (Slide modification):**—An one in 11 dilution of a suitable stock antigen (Astra in preference to Meditec) is prepared with 3.5% sodium chloride solution on a water bath at 56°C in 6" × 3/4" rimless test-tubes. The whole-blood specimens are arranged in racks and one drop of clear serum from each tube is pipetted into each ring of waxed slide by means of pasteur pipette, using one ring for each specimen. Two drops of antigen-emulsion are added to each ring using a pasteur pipette of approximately the same bore as that used for the sera. The slide is slightly rotated and incubated at 37°C, for 25 minutes on a water bath. The results are read off immediately after taking them out of the water bath.

**Reading and reporting of results:**—The results are read under the low power of a microscope using a dim light. The negative sera will show a homogeneous mixture of antigen particles while the positives will show black clumps which vary in size according to

the degree of positivity. The results are read off and reported as positive (+++, or ++), weakly positive (+), doubtful (±) and negative (N).

*The MKLR test on CSF* may be carried out in the same manner. The C.S.F. is pipetted off, 3 drops into the first, 2 drops into the second and one drop each into the 3rd and 4th rings of waxed slide by means of a pasteur pipette. The antigen emulsion (the same as was used for testing sera) is pipetted, one drop each into the first, second and third rings and 2 drops into the 4th ring. The slide is shaken and incubated at 37°C. for 25 minutes on a water bath. The results are read off in the same way as for the sera and the highest dilution showing the maximum clumping furnishes the result.

II. Quantitative tests.—Can be done easily by making serial dilutions of test sera using a known negative serum as the diluent, taking 0.2 c.c. as test serum. Each dilution is tested as for qualitative purposes and the highest dilution showing ++ is taken as the titre.

*The VDRL test*:—An one in 10 dilution of stock-antigen is prepared in a 30 c.c. round glass, or screw stoppered bottle using buffered saline (supplied with antigen) as diluent according to the procedure laid down by the serologist. The clear sera are inactivated and 0.05 c.c. of the serum is pipetted into each ring of waxed slide using one ring for each specimen. One drop of antigen emulsion (1/60 c.c.) is put in each ring by means of a 22 gauge regular bevel or 23 gauge long bevel hypodermic needle attached to an 1 c.c. or 2 c.c. all-glass syringe. The slide is rotated on a VDRL rotator for 4 minutes. In its absence, the slide can be rotated by hand on a smooth surface making 120 revolutions per minute in a circle of 2" diameter.

*Reading and reporting of results*:—The results are read off immediately after rotation in the same way as in the MKLR test with this difference, that the clumps here are brownish in colour and read as P, WP, Df and N and reported as such.

*Quantitative study*:—The test sera are diluted serially, utilising 0.5 c.c. of test serum and using 0.9% sodium chloride solution as diluent, and testing each dilution in the above mentioned manner. The highest dilution giving a positive reaction is taken as the titre. In our laboratory we are following the VDRL procedure, as it does not require negative serum for dilution and 0.5 c.c. of the test serum gives a better dilution than the 0.2 c.c., used in the MKLR test.

*Reporting to physician*:—Views about the proper method of reporting the results to the physician, differ considerably. Some advocate the reporting of results to the physician of each and every member of the battery of tests, done in the laboratory and the physician is expected to make the correct interpretation of conflicting results, if any. This practice, may be helpful only to a few experienced

physicians, but is generally liable to mislead the general practitioner. The opinion of Moore and others which is generally followed, is all in favour of reporting to the physician, only one result (the end-product of all the findings) in which even the specific test techniques employed are not mentioned and the physician is told that the result of the serological test for syphilis (S.T.S.) on the sera sent by him is reactive (positive), doubtful, or non-reactive (negative). *Reactive* means that the reagin present in the blood is detectable by all the tests done in the laboratory; *doubtful* means either it is in too small an amount to be detectable by one test and not by the other, or the laboratory is not sure of its presence in the serum in question; *negative* means that it is absent from the serum and could not be detected by any test-technique. In case a quantitative test is done, the name of the test technique is always mentioned as also the titre.

*Comparative testing* :—It is more or less true that any test-technique performed rightly, will give the same amount of information as any other would have given. The above mentioned newer rapid tests with their attendant advantages compare favourably as regards sensitivity and specificity with the older tests, as judged by the results obtained by the WHO V.D. Demonstration Team at Simla during 1950–51; out of 568 specimens of proved untreated syphilitic sera tested in the above laboratory MKLR, VDRL and Kahn gave the following percentages of sero-positivity :—

	MKLR	VDRL	Kahn
Primary syphilis	97 p.c.	97 p.c.	96.4 p.c.
Secondary „	100 „	100 „	100 „
Latent „	95.7 „	99.7 „	95.5 „
Late „	96.0 „	100.0 „	100.0 „
Congenital syphilis	100.0 „	100.0 „	100.0 „
Average :—	98.2 „	99.4 „	94.5 „

## PART II

### Interpretation of the Results of Serological Tests for Syphilis (S.T.S.) and their Application in Treatment

When the laboratory reports that the S.T.S. on a patient's serum is positive, the question whether the patient is syphilitic or non-syphilitic still remains unanswered because the patient may be really syphilitic, or he may be one of the non-syphilitic reactors. It is towards sifting of the latter group of patients that this discussion is aimed at.

The false positivity may be due to technical errors in collecting and labelling samples, in the actual performance of the tests and in the reading and reporting of the results; or it may be a biological one, which means that (1) The reagin which, like other antibodies, is associated with the gamma-globulin fraction of the serum (a) is

present in such a large amount as to give positive results in an otherwise normal person, a fact with an 1 in 2000 or so incidence; (b) is being produced by non-syphilitic influences in such a large amount, particularly in those having hyper-gamma globulin in their blood, as to be detectable by the tests performed. This takes place in 15 to 20% of the population. (2) There is an increase in or alteration of some chemical substance in the blood, such as would favour the reaction.

Some of the common conditions giving rise to a biologically false positive reaction (B.F.P.) which will require to be excluded are:—leprosy, malaria, kala-azar, vaccination against smallpox, infective hepatitis, infectious mono-nucleosis, virus-pneumonia, pneumococcal-pneumonia, advanced tuberculosis, respiratory disease including the common cold, measles, mumps, spirochaetal diseases, *e.g.*, rat-bite fever, relapsing fever and Weil's disease. In addition S.T.S. will be positive in other spirochaetal diseases resembling syphilis *e.g.*, bejel, pinta and yaws.

The majority of such false positive reactions are weakly positive or variable and usually disappear within 3 to 6 months. There is as yet no laboratory procedure other than the treponemal-immobilizing-test (TPI), which can differentiate between false and true reactors. Hence it must be emphasized that:—"A single positive serological reaction not supported by clinical evidence and a conclusive case-history, does not necessarily mean syphilis and must be regarded as an indication for the necessity for further investigation."

The procedure recommended for the interpretation of positive S.T.S. is to determine its true significance by correlating the following obtainable facts:—(1) history of exposure followed by lesions attributable to early syphilis, its behaviour towards treatment and its further development etc.; (2) a thorough examination of all systems, including a dark-field examination of suspected lesions, not only to detect the minutest evidence of syphilitic lesions present but also to exclude those conditions known to be producing B.F.P. results; (3) an epidemiological investigation including the examination and S.T.S. on all contacts, on the sexual partner and children; (4) the determination of the height of reagin level by repeated quantitative tests. A falling titre in the absence of any anti-syphilitic treatment usually means B.F.P. reactor.

Apart from the above, the pregnant woman with a positive S.T.S. especially in the later half of her pregnancy must be treated, so as to minimise the risk of conveying syphilis to the new-born. In some persons, a prolonged follow-up to exclude B.F.P. may seriously injure the patient psychologically; to avoid this from the practical point of view, Paillard and Bolay suggest that it would be better to have "an end with terror rather than have terror without an end" and it would be advisable to treat such cases with penicillin alone or penicillin and bismuth and to avoid

the use of salvarsan preparations. A final answer cannot yet be given to the question of persistent biologically false-positive reactors.

**Quantitative reactions.**—Quantitative reaction is not an aid to diagnosis except when it is used to differentiate a true from a false positive reaction but it merely determines the dilution in which that particular serum continues to give a positive reaction.

In syphilis a high or low titre does not indicate the measure of gravity of the syphilitic infection. Considerable damage is done to the patient by the doctor who explains to him that two plus is much better than four plus and so on. A patient whose serum gives a positive reaction with one in eight dilution is no less syphilitic than a patient whose serum gives a positive reaction with an one in sixtyfour dilution. The chief value of the test lies in the fact that the physician can evaluate a serologic response in his patient to a particular treatment-schedule from the beginning of the therapy throughout the period of clinical and serologic follow-up. A reduction in serologic titre in the same patient indicates the success of the previously administered anti-syphilitic treatment.

Carefully performed quantitative reactions are useful to the physician.—(1) to differentiate between true and false positive reactions; (2) to differentiate between serologic relapse or reinfections:—in serologic relapse serologic titre rises before any clinical manifestation is noticed and but reinfection, clinical manifestations may appear even before the rise in the serologic titre except in asymptomatic reinfections; (3) as a guide in judging the response to treatment:—after allowing for other considerations, a falling titre in the same patient following a definite schedule of treatment is indicative of improvement. The persistence or a rise of the titre long after the treatment must be viewed with doubt as to the efficacy of the treatment given; (4) to differentiate between prenatal syphilis and syphilo-toxæmia in the newborn:—if, in a newly-born child the serologic titre has a tendency to rise within the first three to four weeks in the absence of anti-syphilitic treatment, it is indicative of prenatal syphilis. On the other hand, if the serologic titre decreases with the lapse of time, it signifies syphilo-toxæmia. It is worth noting, that due to the fact, that only univalent antibodies are passively transferred from mother to foetus through the placenta, the non-syphilitic infant born to a syphilitic mother may give a positive result with the complement-fixation tests and negative with the flocculation tests. A really syphilitic child will however, give positive results with both tests due to its being able to produce bivalent antibodies in its blood.

**False negative results.**—Apart from the false positive reactions referred to, we may also get false-negative reactions which may be found in:—(a) early primary syphilis (sero-negative primary

syphilis); usually it takes 3 to 4 weeks after infection for a patient to show reactivity to routine S.T.S.; (b) late syphilis: in certain cases of late syphilis such as cardiovascular or neurosyphilis, one may get a negative S.T.S. e.g., tabes dorsalis with 30–50% of sero-negativity; and (c) late latent syphilis:—S.T.S. may be negative in an appreciable percentage of such cases.

Sero-negativity depends upon:—(1) the presence of too small an amount of antibodies detectable by routine tests; (2) the excess of antibodies in certain cases yielding negative results due to prozone phenomenon; (3) the use of serologic tests with low sensitivity; (4) the presence of a thermolabile or thermostable and inhibiting factor in the serum.

*S. T. S. on C. S. F.*—A positive S.T.S. on C.S.F. gives positive proof of neurosyphilis, because false positivity in this case is far less frequent than in the blood and is found in all conditions, like brain-tumour, sub-arachnoid hæmorrhage and meningitis (coccal, tubercular, acute lymphocytic choriomeningitis) which can easily be differentiated clinically. Complement-fixation tests, are more reliable in this case than flocculation tests. Moreover, a negative S.T.S. on the cerebrospinal fluid does not exclude neurosyphilis.

*Serologic response in treated cases of syphilis depends upon.*—

1. *The treatment schedule*:—In penicillin-treated cases, the higher the total dosage of penicillin (up to a certain limit) and the longer the duration of treatment, the earlier the S.T.S. will revert to sero-negativity; there may however, be exceptions to this.
2. *The state of the disease*:—The more long-standing the disease, the longer time will a patient take for attaining sero-negativity. A rough idea can be formed from the following when successful treatment has been administered:—(a) sero-negative primary syphilis will not usually become sero-positive; (b) sero-positive primary syphilis and secondary syphilis will revert to negativity in most cases, within 6 to 9 months, except when positive in high dilutions; (c) early latent syphilis of less than six months' duration will take about one year, while that of more than six months' duration will take one to two years to revert to sero-negativity and (d) late syphilis or late latent syphilis of more than two years' duration will take many years to attain sero-negativity.
3. *The serologic titre*:—The higher the titre, the longer will it-usually take to attain sero-negativity.
4. *The immunologic response of individual patients*:—Patients developing exceptionally more antibodies revert to sero-negativity, later than those forming fewer antibodies under the same conditions.
5. *The sensitivity of the tests*:—The more sensitive tests remain positive longer than the less sensitive ones.

Re-treatment of syphilitic patients—Although a persistence of serologic positive reaction does not necessarily mean persistence of

the infection, retreatment of syphilitic patients is indicated : (a) if S.T.S. remains positive long after it is anticipated to be negative or there is no appreciable fall in titre within a reasonable time as determined by quantitative tests ; and (b) if the patient develops clinical or serological relapse or reinfection.

*Sensitivity and specificity of the tests* :—The sensitivity of a test means its ability to produce positive results in syphilitic patients, while the specificity of a test denotes its ability to give negative results in presumably non-syphilitic cases. An ideal test should therefore, be cent per cent sensitive and cent per cent specific ; this ideal has however, not yet been achieved. The order of sensitivity and specificity of the more common tests in use, is given below in descending order.

Order of Sensitivity.	Order of Specificity.
No. 1. MKLR and VDRL (of nearly equal sensitivity).	Kahn.
No. 2. W. R. performed with crude antigen.	W. R. performed with cardiolipin antigen.
No. 3. W. R. performed with cardiolipin antigen.	W. R. performed with crude antigen.
No. 4. Kahn.	VDRL
No. 5. —	MKLR.

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#### Fatal Aplastic Anæmia

Winternitz of San Francisco describes the clinical history and the results of necropsy in a woman, aged 35, in whom fatal aplastic anæmia, developed following treatment with chloramphenicol. The possible etiological relationship of a pre-existing chronic glomerular nephritis and coexisting hepatitis is discussed. The author stresses the importance of the close observation of the hæmatopoietic system during the administration of chloramphenicol.—(*Calif. Med.*, 77 : p. 335: Abst. *J.A.M.A.*, 21-2-1953).

## CERTAIN CLINICAL CONSIDERATIONS ON THE CHEMOTHERAPY OF CHLOROMYCETIN\*

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**Introduction.**—Chloromycetin, which is considered the best among the antibiotics of today plays a significant role in modern chemotherapy. It has opened up a new era in the treatment and control of infections due to a wide range of gram-negative and gram-positive organisms. The viricidal and rickettsicidal properties of chloromycetin are noteworthy.

**Evolution of the drug.**—Chloromycetin a pure colourless, bitter, stable, crystalline, substance was isolated by Burkholder, Ehrlich *et al* in the year 1947 from "*Streptomyces Venezuelea*" obtained from the soil in Cascaras. This mould can be grown in submerged aerobic culture on a commercial scale.

The production of chloramphenicol from "*Streptomyces Venezuelea*" is also enhanced by adding molasses and yeast to the culture medium—a method used in the manufacture of the drug on a commercial scale synthetically.

**Therapeutic activities of chloromycetin.**—Chloromycetin has a high therapeutic activity on many gram-negative and certain gram-positive organisms as well as on viruses and rickettsial bodies. How the drug acts is not yet clearly known, but its bacteriostatic and bacteriolytic activities in human-beings without producing serious toxic effects have made it a really valuable therapeutic agent.

Chloromycetin is noncumulative in its effect. It is absorbed rapidly from the gastro-intestinal tract and about 10% of the daily total dose is excreted in the urine. The peak blood-level of the drug is reached in 2 to 3 hours after administration. Chloromycetin differs from the other antibiotics in that the organisms do not develop drug-resistance.

Chloromycetin is equally effective in children and in adults. The advantage of this drug over other antibiotics in paediatric practice is its being very acceptable to infants and children owing to its pleasant flavour.

The prophylactic value of chloromycetin lies in its bacteriostatic activity on the intestinal flora and its ability to inactivate and eliminate most of the pathogenic organisms prior to surgical intervention in acute pelvic inflammatory conditions (Altemier and Giuseffi). Redewill advocates the prophylactic use of chloromycetin before radical operation for the removal of the prostate gland, as the drug may make vasectomy unnecessary by preventing post-operative epididymitis. The febrile stage in the acute inflam-

\* From a paper read at the XIX Andhra Medical Conference at Masulipatnam on 3-5-'53.

matory diseases of pelvis in most cases terminates within 72 hours after the institution of treatment with chloromycetin. The patient is thus rendered surgically fit within 3 days from the commencement of therapy. Chloromycetin is compatible with other allied antibiotics and may therefore, be used in conjunction with other chemotherapeutic drugs in refractory cases with eminently satisfactory results.

**Routes of administration.**—Chloromycetin is effective by whatever route administered. The following are some of the several modes of using the drug:—(1) Ingestion, (2) Injection, (3) Infiltration, (4) Irrigation and (5) Inunction.

The dosage differs with the age of the individual, the route of administration, the clinical indication, the severity of infection and the resistance of the patient to bacterial invasion.

*Ingestion* is the best route as the majority of cases respond only to oral treatment. The usual adult dosage by this route is about 20 mg. per lb. of body weight per day in divided doses at regular intervals during the period of acute exacerbation of infection. During the afebrile period, half of the original dose (10 mg. per lb. of body weight per day) would suffice. A total minimal dose of 12 to 15 g. is suggested in acute infections. In children however, the dosage is limited to 50 to 100 mg. daily per kg. of body weight during the acute stage and after combating the infection and controlling the symptoms, maintenance therapy is instituted with 30 to 50 mg. doses daily per kg. of body weight. To facilitate administration to infants and children, 50 mg. capsules have also been placed on the market.

Chloromycetin is administered also per rectum. The capsule is punctured in several places and inserted in the rectum after thoroughly cleansing it with an enema. The buttocks are held in apposition for 5 minutes to ensure proper retention of the kapseal in position; when given in this way, the dose should be increased by 25% above the oral dose.

*Injection* treatment with chloromycetin is also in vogue. The drug is administered intramuscularly, as well as intravenously. A 25% solution of chloromycetin in acetyldimethylamine is injected deep into the gluteal muscle (the upper and outer quadrant of the thigh). The same solution well-diluted in glucose or saline is used for intravenous injections; the mixing and dilution of the drug should be carefully controlled so as to prevent floating and precipitation. The simultaneous administration of chloromycetin orally and parenterally has much to commend it.

Chloromycetin is also used for *topical application* in localised infective lesions, as it has been found to be more effective when applied locally, than when used orally. This effect has been of immense value in preoperative, operative and post-operative dressings. The topical applications of chloromycetin, are as under :—As

*a lotion*:—The contents of 4 capsules (1000 mg.) of chloromycetin are added to 5 c.c. of distilled water and used for irrigation. *As dusting powder*: The contents of 4 capsules are mixed with one ounce each of zinc oxide and pulv. amyllum and infiltrated at the site of the wound. *As ointment*:—The contents of 2 capsules are mixed in 2 ounces of vaseline and used for inunction.

Chloromycetin is reported to have been administered by the stomach tube when oral medication became impossible due to loss of consciousness. The striking feature was that within 48 hours after such introduction the patient regained consciousness.

Clinical considerations re : Chloromycetin.—Chloromycetin is of great value in the treatment of *typhoid fever*. The clinical response in this fever depends on the stage of fever in which chloromycetin is sought to be administered. If treatment with chloromycetin starts soon after the onset of the fever and is continued sufficiently long after the fever remits, uneventful recovery usually takes place. If the treatment is started on the appropriate dose-schedule on the ninth day of the onset of fever, the patient experiences a defervescence by the 11th day, becomes afebrile on the 12th day; and normal activity may be resumed on the 15th day after the onset of fever. The treatment should always be continued for some time even after the afebrile stage is reached. If the patient becomes afebrile on the 3rd day chloromycetin should be continued for not less than a week. Inadequate treatment of typhoid fever with chloromycetin tends to produce relapses which can be cured successfully with larger doses of the same drug given for a suitably long period. Usually 3 gm. per day in divided doses for 5 days effects a certain cure in relapses of typhoid fever. Regarding the optimum dosage-schedule for the treatment of typhoid fever, an adequate concentration of chloromycetin in the blood is necessary to effect a cure; and the minimum effective concentration in the blood has been found to be 10 mg. per c.c. Clinical experience indicates that an initial dose of 2 mg. per day in divided doses for two days in the case of adults is necessary to combat the infection and alter the course of the disease. This should be followed by treatment with one capsule every 3 hours until the patient becomes afebrile—usually 15 g. is required on an average over a period of 6 days. Rapid clinical response is seen within 3 to 5 days of starting the treatment. Even after the temperature has come down, the treatment should be continued with 1 capsule every 6 hours. Intervals of 6 hours or less assure a concentration of the drug above the minimum effective level. The drug should not then be repeated at intervals of less than 6 hours.

A 'loading dose' is not necessary to effect a cure. Massive doses of the drug may lead to a rapid and massive death of the pathogenic bacteria in the system resulting in a liberation of endotoxins that might induce a severe anaphylactic shock. During

chloromycetin therapy of typhoid fever complete physical rest is essential. No physical activity nor any indiscretion in diet should be permitted.

Infections of the respiratory tract, have yielded remarkably well to this therapy. Gray observes "chloromycetin completely sterilizes the mucous membrane of the upper respiratory tract." It has a broad-spectrum activity, against the organisms responsible for affections of the respiratory passages, *e.g.*, diplococci pneumoniae, staphylococci, streptococci, astrococci, coryne bacterium, haemophilus and other rickettsiae and viruses producing pneumonic infections. The dosage of chloromycetin in respiratory infections varies with the type of infection, the degree of damage to the tissues and the age of the patient. Usually a dose of 50 mg. per kg. of body weight per day in divided doses should be administered till the symptoms subside. During convalescence, half the original dose *i.e.*, 25 mg. per kg. of body weight per day in divided doses would suffice. The response to the drug on the above dosage-schedule is rapid—the patient becoming afebrile within 18 hours after institution of treatment; the treatment should however, be continued for 8 days using 3 g. per day in divided doses. Younger people seem to require larger doses than the older ones, for obtaining the optimal therapeutic effect. Clinical observations show that in the treatment of a pneumonic infection an initial divided dose of 3 g. followed by doses of 0.5 g. four times daily for a period of 4 days is necessary.

In pertussis an initial dose of 0.25 g. should be followed by 0.125 g. three times daily for 4 days (or till the cough count is depressed and the course of disease gets limited). This should be continued for a further week at intervals of 12 hours, the dose being 0.125 g. This schedule for pertussis applies mainly to infants of less than six months.

In venereology.—Chloromycetin has been used with success. In cases of gonorrhoeal urethritis resistant to penicillin therapy, chloromycetin acts well. A single oral dose of 3 g. followed by doses of 1.0 g. t.d.s. for 2 days, produces marked improvement in cases of gonorrhoeal urethritis. In granuloma inguinale 30 g. of the drug in divided daily doses for 10 days has done well, the recurrence rate being much smaller than with other antibiotics. Delayed relapses are noticed with inadequate treatment. Therefore, treatment in these cases should be by the oral as well as parenteral routes. This may be done without fear of untoward reactions. In chancroid, chloromycetin is said to act very well synergetically with penicillin. In the case of chancroid, larger doses of 0.5 g. 4 times a day for 13 days promise good results. In the treatment of lymphogranuloma venereum, an initial dose of 0.5 g. with a daily total dose of 2 g. over a period of 15 days effects a complete cure. This dose-schedule depends of course, on the extent of damage to tissues and

the rate of response to treatment. A divided dose of 1 g. per day for 2 weeks followed by a dose of 0.5 g. daily for three months is the most suitable for the treatment of lymphogranuloma venereum.

Rectal lesions readily heal and strictures enlarge very early even within 24 hours of starting chloromycetin therapy. Chloromycetin obviates the need for colostomy and even in cases of permanent colostomy regression of the rectum occurs permitting a closure of the cavity.

In primary and secondary syphilitic lesions a loaded dose of 1 g. every six hours up to a total of 50 g. given under expert medical supervision yields excellent results. Romansky *et al* showed in 32 dark-field-positive cases of syphilis that a daily dose of 30 mg. per kg. of body weight up to a total of 10 to 25 g. produced good results. *Treponema pallida* disappeared completely within 24 hours of treatment. Early cases of syphilis responded better than the late ones. In view of the necessity for massive doses in the treatment of syphilitic conditions it is always better to hospitalise the patient during treatment. Chloromycetin is also effective in cases of genital inguinal lesions in proctitis.

Some advocate chloromycetin therapy in dermatological conditions. Chloromycetin has been found to be successful in the treatment of herpes zoster, varicella, impetigo contagiosa, furunculosis, folliculitis and other dermal lesions due to viral infections. In herpes zoster, relief of pain is obtained in about 4 hours after the administration of an initial dose of 0.5 g.; marked improvement occurs in 3 days, following treatment with doses of 0.25 g. given every 4 hours. A total dose of 6 to 8 g. usually suffices to effect a complete cure.

Chloromycetin has been used extensively in ophthalmology and found to act wonderfully well in external ocular infections. Locally applied, it penetrates the ocular tissues and fluid very rapidly and counteracts infection. By allaying irritation it has a soothing effect on the cornea. If chloromycetin ointment in a vaseline base causes irritation, an aqueous solution (25 mg. per c.c.) must be substituted as it allays irritation and soothes the cornea. Chloromycetin is highly efficacious in the treatment of trachoma. An initial oral dose of 3 g. on the 1st day in 6 divided doses followed by 250 mg. 3 hourly for the next 4 days, together with the simultaneous instillation of the solution in the eyes reduces photophobia, and lacrimation and corrects inflammation and opacity of the cornea. In obstinate cases offering resistance to the drug probably due to a secondary bacterial invasion, sulphonamides may be used as adjuncts to chloromycetin for effecting a complete cure. Chloromycetin is effective also in dacryocystitis, keratitis and in all forms of conjunctivitis.

Chloromycetin has been tried with good results in gastroenterology. It has a definite inhibitory effect on the intestinal flora. A

daily dose of 3 g. should be given till symptoms of abdominal discomfort, mucus and blood in motions and griping pain subside and till the action of the sphincters is controlled. Then a maintenance schedule should be followed at intervals and with a shorter course.

In amœbiasis, 0.5 g. thrice a day after meals for 6 days gives good results. In salmonella enteritis, gastroenteritis, infantile diarrhoea and cholera also, chloromycetin is reported to be effective. In brucellosis a total amount of 20 to 25 g. given over a period of 10 days in divided doses is indicated. In cases of caecal and appendicular pain however, the treatment should be prolonged for 8 to 10 days.

In pelvic inflammatory lesions it is reported to have given wonderfully good results. It is an antibiotic of proved efficacy in cases of septic abortions, puerperal sepsis and in preoperative, operative and post-operative conditions of surgical affections of the male and female pelvis. Chloromycetin is successfully employed in cases of intestinal hæmorrhage, perforation, peritonitis and pelvic cellulitis.

Opinions differ, regarding its value in the treatment of affections of the urinary tract. In fact, no single antibiotic has been found to be universally effective in urinary tract infections. In pyelonephritis, most organisms are susceptible to chloromycetin but when they get resistant, the use of penicillin as an adjunct will be necessary. Chloromycetin therefore, acts only as an adjunct in the treatment of urinary tract infections after the removal of calculi, obstructions and other foci of infection. A dose of 250 mg. four times daily for 7 days is ordinarily sufficient for the treatment of pyelonephritis. Treatment should be continued until symptomatic relief is obtained or until operative measures have eradicated the foci of infection.

In otorhinolaryngology, where bacteria, viruses, and rickettsial bodies have all got their share in producing ear, nose and throat troubles, chloromycetin is very useful and treatment should continue for 3 days, though abatement of symptoms occurs rapidly with a daily divided dose of 2 g.

Chloromycetin has been acclaimed to be the only drug having *specific chemotherapeutic rickettsicidal and viricidal properties*. Chloromycetin is very effective in Rocky mountain spotted fever, Q' fever, murine typhus, scrub typhus, rickettsia pox etc. The treatment in these conditions shows a defervescence within 12 hours of medication. The following virus infections readily yield to chloromycetin therapy:—psittacosis, pneumonitis, lymphogranuloma venereum and atypical pneumonia.

Chloromycetin is not without side-effects. As already stated an initial 'loading dose' sometimes leads to a massive and rapid death

of pathogens, thereby releasing endotoxins into the blood and producing anaphylaxis. Though gastrointestinal, neurotoxic, cutaneous and allergic reactions are *not very common*, anæmia, anorectal complications, vaginitis and dermatitis sometimes occur; but these can be controlled by stopping the drug and using anti-allergic agents.

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### *Hæmatopoietic Depression Induced by Chloramphenicol*

Erslev reports two cases in whom treatment with chloramphenicol (chloromycetin) was considered responsible for erythropoietic depression.

The first had been in good health until three weeks before hospitalization, when he developed diarrhoea and fever. The diarrhoea subsided temporarily after administration of paregoric and penicillin for two days. However the fever continued, and 10 days before admission, he had a fresh attack of diarrhoea with almost black stools. He was given sulphamerazine for five days, but his condition continued to deteriorate and he was admitted to the hospital in a semi-comatose state. During the first three days, he was given blood and aureomycin; when the diagnosis of typhoid was established, treatment with chloramphenicol was begun, a total of 85.5 gm. being given during a 25-day period. The patient became afebrile, but the faecal cultures continued to yield *B. typhosus*. A few days after chloramphenicol was discontinued, the patient again became febrile and a second course of the drug was initiated, 70 gm. being given in a 19-day period. Thus this patient received a total of 155.5 gm. of chloramphenicol. In the second patient blood culture and bone-marrow culture were positive for salmonella and this patient received a total of 66.5 gm. of chloramphenicol in 24 days. Anæmia and hypoplasia of the erythropoietic bone-marrow tissue were observed in both patients. Other drugs had been given prior to and during chloramphenicol administration but when chloramphenicol was discontinued a striking reticulocyte response occurred along with the reappearance of normoblasts in the bone-marrow. This sequence indicates a *direct relationship between the administration of chloramphenicol and the erythropoietic hypoplasia*. Chloramphenicol contains a nitrobenzene ring and from the beginning of its clinical use in 1948 it was considered a potential bone-marrow toxin. So far, forty cases have been reported in which the administration of chloramphenicol was followed by maturation-arrest or hypoplasia of bone-marrow elements; 27 of these terminated fatally. This hæmatopoietic bone-marrow depression is still considered a rare complication of chloramphenicol therapy. However, Wilson found it in 2 of 82 treated cases; Lindau in 3 of 8 cases, and both cases reported here were discovered within one month. Hæmatological observation is necessary in all patients who receive chloramphenicol, and the drug must be stopped promptly, if there are any signs of bone-marrow depression.—(*Blood*, N.Y., 8, 170-174, 1953, Abst., *J.A.M.A.*, 2-5-1953).

## CLINICAL DIAGNOSIS OF THE DYSENTERY SYNDROME\*

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Poona.

IN general practice, diagnosis of diseases is usually made on clinical grounds alone for want of adequate laboratory facilities on a large scale. The diagnosis of the dysentery syndrome, made on clinical grounds only, however carefully made cannot be definite and absolutely accurate as a number of related and unrelated clinical conditions simulate the dysentery syndrome. This limitation in clinical diagnosis should therefore, be always kept in mind. It will be unsafe and dangerous to persist with specific treatment for days and months without confirming the clinical diagnosis by laboratory, X-ray and if possible, sigmoidoscopic examinations. Many tuberculous infections and many malignant neoplasms are often missed in their earlier phases, because of the unwarranted reliance placed on clinical diagnosis alone. In a large majority of cases, unresponsiveness to modern treatment results from wrong diagnosis.

Dysentery literally means a painful movement of the bowels. Bowel movements which are not painful, are usually not dysenteric even though frequent. Thus diarrhoeas may occur with and without pain during defaecation. By mere inspection of the motion, it is usually possible to have some idea whether it is from the small or the large bowels. Large bowel diarrhoea is characterized by semi-solid faeces with griping and mucus. The small bowel diarrhoeas are characterized by green liquid watery motions and any abdominal pain present is not related to bowel movement, but occurs independently. The number of stools may vary from patient to patient and much reliance cannot be placed on it. In cases with an acute onset, inquiry should always be made whether the patient had recently returned from any journey or pilgrimage and whether any others in the family had similar attacks in the past. Correct information is often deliberately suppressed out of fear that the patient may be removed to a hospital if some infectious and epidemic disease like cholera, is suspected. Diarrhoeas may also be classified according to whether they contain blood or not. The colour of the blood will depend on the site of its origin as well as on the rapidity of the evacuation. Blood when it comes from the ano-rectal region is bright red, and is not necessarily accompanied by diarrhoea. There may be pain, but it is not diffuse and generalized but localized to the rectal region. The lesions of the small intestines are conspicuous by pain which is felt round about the umbilicus in the upper abdomen. Pain in lesions of the large bowel is usually confined to the pelvic portion and is always present during defaecation. Sometimes pain is

\* Specially contributed to THE ANTISEPTIC.

felt after a meal, as occurring over the ascending or descending colon. This is really an exaggerated gastro-colic reflex brought into consciousness as pain, due to an inflamed condition of the large bowel or stomach. Such pain in and around the umbilicus, or over the large bowel is not present in lesions of rectum, in which tenesmus is the characteristic feature. When analysed it is found to consist of pain not only during defæcation but even when not defæcating. A sensation of a foreign body in the rectum, with unsatisfied bowel movement and the constant urge to pass more and still something more with violent straining, characterise the condition. In debilitated and aged persons such straining in the squatting position may produce œdema in the feet. Tenesmus is always present in bacillary dysentery. Pain may also be produced in dysentery by involvement of the peritoneum, the inflammation reaching it through the entire bowel wall. Under these circumstances there is not only pain but localized tenderness over the affected portion; the pain may then become severe with exertion, due to a drag on the mesenteric attachment. Colicky pain is not only limited to intestinal, biliary or renal colics, but may be produced by intrathoracic spinal and vascular lesions. Vascular lesions like mesenteric embolism also exhibit blood in the stools and it is always worth remembering that blood in the stools does not necessarily always mean amœbic or bacillary dysentery but may be due to a variety of causes. On the other hand, blood may be absent in mild cases of dysentery. Piles may also start bleeding after any inflammatory condition of the bowel. Mucus in the stools is of little help in diagnosis, because it is usually present in all conditions of large bowel irritation howsoever produced. Mucus is common in diarrhœas associated with para-enteric infections, worms and psychogenic disturbances.

The dysentery syndrome being exceedingly common, correct diagnosis becomes a real problem to the physician. The following are cases where a straightforward diagnosis cannot be readily made:

I. Dysentery.—Amœbic or bacillary is the commonest. Acute onset, frequency of stools, presence or absence of fever, pain, whether colicky and occurring in waves, or dull and felt along the large bowels, tenesmus and its severity, character of the stools, its colour, smell, stickiness, whether fœcal or watery, the character of the blood when present, the character of the mucus, watery or gelatinous, sticky or frankly purulent are all points on which the clinical diagnosis has to be based. There is no single clinical finding which is exclusively characteristic of either the amœbic or bacillary type. The sequence in bacillary stools is "very frequent, frequent, then tenesmus, sticky and scanty." Amœbic infections are notorious for recurrences. Either type may assume a fulminating course and clinical diagnosis alone is useless; no time should therefore, be lost in securing a laboratory report. However, if there is acute diarrhœa with blood and mucus associated with griping, and

there is some rise in temperature, a provisional diagnosis of bacillary dysentery may be made in the majority of cases. The presence of tenesmus and typical sequence of progress of bacillary infection confirm the diagnosis. In cases, where a clinically definite diagnosis cannot be made and the help of laboratory is not readily forthcoming, it is best to use a combined therapy of suitable sulphadiazine and an amoebicidal drug like enterovioform or didoquine or emetine in very severe cases.

In chronic cases, bacillary dysentery recedes into the background and the amoebic assumes greater prominence. I feel that in chronic cases the clinical diagnosis should always be confirmed, because different forms of colitis have a similar clinical pictures and it is not therefore, always possible from clinical findings alone, to be sure of the causative agent. Chronic dysentery being much more common takes the first place in diagnosis. A satisfactory response to antidyenteric treatment should not always be interpreted as a correct diagnosis, since other forms of colitis also have remissions and many times coincidences do occur. Chronic amoebic dysentery has elusive symptoms and vague indefinite abdominal signs. Essentially the presenting symptom is irregular diarrhoea with blood and mucus, off and on. Neglected cases may show dehydration marked wasting and severe anaemia. There may be a history of alternating constipation and diarrhoea, and severe constipation as a sequela is not unknown. Anorexia, flatulence, dyspepsia, neurasthenia usually accompany irregular diarrhoea. Pain is variable both as regards location and severity. It may come on first thing after food, explained by the normal gastrocolic reflex becoming painful. It may also mimic subacute appendicitis.

Intestinal parasites may be the cause of the dysenteric syndrome, or they may coexist and make the case severe. Round worms come to mind quite readily as the cause, specially in children with large abdomen, pale appearance, irritable temper, teeth-grinding and nose-picking. In adults symptoms of duodenal ulcer and gall bladder disease may be observed. He is indeed a wise physician who tries a suitable vermifuge in chronic gastrointestinal disease. *Balantidium coli* cause a clinical picture which is hard to differentiate from chronic amoebic dysentery. Flagellates like giardia, lamblia produce recurrent periodic diarrhoea not usually accompanied by griping or tenesmus; this is not really colitis but enteritis resulting in frothy pale bulky stools with a variable amount of mucus.

The diagnosis of nonspecific ulcerative colitis wholly on clinical grounds is impossible. In common with chronic dysentery there is griping, tenesmus, blood and mucus but in addition there is an admixture of pus. The course is usually downwards, punctuated at irregular intervals with remissions and exacerbations. It is only

after several negative laboratory reports and an X-ray picture showing absence of haustral marking can a diagnosis be made. The patient is usually a chronic invalid.

A rare case of dysenteric syndrome is thrombosis of the mesenteric vessels. The patient is generally suffering from some form of chronic cardio-vascular disease. The characteristic symptom is agonizing pain over the abdomen very much unlike the pain in any type of dysentery. The pain is unbearable and the patient screams with pain. There is tenderness and rigidity. The frequency of stools mixed with blood usually tarry in colour, may mislead the unwary. The prognosis is very bad.

Intussusception is another condition likely to cause confusion. Frequent motions with blood and mucus, tenesmus and straining are features which closely resemble dysentery. The onset is sudden in both. In intussusception faecal matter is very scanty. But the most arresting feature is not the diarrhoea with blood and mucus but the paroxysm of excruciating pain at frequent intervals. The presence of a recently developed abdominal tumour may be ascertained before much distention has occurred. Fever is late in appearing. Prostration increases rapidly. Treatment is sought not so much for the dysenteric syndrome but for the attacks of pain with which the child screams. Even between the paroxysms the child is very restless.

Tubercular lesions of the intestinal tract are found usually around about the ileo-caecal valve. The symptoms are those of ileo-colitis. There is chronic diarrhoea with a variable amount of blood, tenesmus and colicky pain. The pain and tenderness, when present is in the right lower quadrant, and not over the whole area of the large intestine. There may be thickening in the caecal region. The onset is slow, there is no definite acute attack to start with, the course is chronic and progressive without any remissions. In chronic amebiasis there is usually a history of a first acute attack, the course showing relapses and remissions. In tubercular infection the onset is insidious and in the beginning the only noticeable change is the disturbance in the normal rhythm of stools, to be soon followed by bouts of alternating diarrhoea and constipation. The stools are very foul smelling. The clinical diagnosis of tubercular infection becomes more certain when chronic peritonitis or enlargement of mesenteric gland or other lesion in other parts of the body are found. In the absence of these there can only be a reasonable suspicion which may be confirmed by X-rays and laboratory tests.

Henock's Purpura (purpura fulminans) may produce a picture which may superficially resemble the dysenteric syndrome. The pain is not however, of a griping nature being more diffuse over the upper abdomen and not specifically related to defaecation. Some particular kind of food might have precipitated the attack and a history of similar attacks may be forthcoming. Abdominal

pain is of a colicky nature. Urticaria, œdema and joint involvement when present will materially aid in the diagnosis. The acute attack is associated with fever, leucocytosis and eosinophilia. Under these circumstances the onset of some acute infection is suspected but the quick subsidence of the condition on removal of the offending agent, will establish the diagnosis. Local rectal conditions like piles produce bleeding but the patient usually recognizes this and his presenting complaint is bleeding or pain referred mainly to the anorectal region and not the dysenteric syndrome. However as above mentioned with slowly developing lesions, the dysenteric syndrome may be manifest. A rectal examination must be made to ascertain the existence of a local lesion.

Sprue, pellagra, anæmia, vitamin deficiencies, parenteral infections, also produce diarrhoeas. Blood and mucus are not present. Many of these conditions are associated with varying degrees of abdominal distress but not griping. A little mucus may however, be present, probably due to irritation of the large bowel, secondarily set up by the diarrhoeic stools. Psychogenic diarrhoea is often associated with mucus. Clinical diagnosis is an art which can be learnt only by following some well-defined scheme of examination, taking all the symptoms and signs into consideration and then interpreting them. Confirmation by laboratory and other specific tests should always be attempted, as even experts are liable to err, particularly in the diagnosis of this group of maladies.

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### Toxicity of Chloromphenicol

Administration of chloramphenicol may result in aplastic anæmia or other side-effects including anaphylactic reactions, cutaneous eruptions, moniliasis, and irritation of the mucous membranes. Lasky *et al*, *J.A.M.A.* 151: 1403, 1953) describe a case of bacterial endocarditis in which the administration of 6 g. of the drug daily for six weeks led to a severe anæmia followed by retinal hæmorrhages and bilateral optic neuritis. After discontinuing the drug, the anæmia disappeared but the vision remained seriously and permanently affected. This report should not however, deter doctors from using the drug; for in this case the dosage was very large and it was administered over a long period. Compounds containing a benzene ring with a nitro-group attached—as in chloramphenicol—are known to be potentially toxic. In moderate dosage and for short-term administration, the drug is safe enough; but the use of other antibiotics should always be considered if medication has to be long continued.—(*Annotation in Lancet*, 20-6-1953).

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## HEAD INJURIES\*

M. N. PALADHI.

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I. Scalp.—Simple swellings, abrasions, bruises and cut wounds usually occur on the scalp. The brain may be injured by fracture of the skull resulting in contusion, laceration, concussion or compression without any scalp injury. Sometimes blows from blunt weapons cause rupture of the inner surface of the scalp and not its outer surface. Large flaps of scalp are often torn off by machinery, by mauling caused by beasts, and by blows from long cutting weapons and through other accidents.

Wounds caused by blunt weapons may simulate incised wounds. They should be examined with a magnifying glass in broad daylight. The cut edges of the contused wound are not sharp, the hair bullae are crushed and strands of tissues are found across the breadth of the wound, which in the case of incised wounds are found to be cut across. All scalp wounds, whether incised, contused or lacerated bleed freely.

TREATMENT:—Brushing and disinfection by normal saline or other non-irritating antiseptic drugs such as acriflavine, mercurochrome, penicillin etc. should be done. The edges should be pared in case of laceration and then sutured. When the wound is deep in the pericranium, a small rubber drain should be left in for a day or two. If left open without suturing there will be great delay in healing and disfiguration may occur.

II. Skull.—(a) Fractures of the vault occur at the site of direct violent contact or on its opposite side by *contre coup* (*counter-side*) when the head is not supported. They are usually caused by heavy blunt weapons, falls from heights or from moving vehicles, by the impact of heavy weights on the head, or by the passage of the wheel of a motor car over the head. Sometimes fracture of the skull bones is caused without any contusion or open wound on the scalp, though an extravasation of blood on its under surface may be present. Rarely indirect violence i.e., fall on the heels or fall in a sitting position may cause a fracture of the base of the skull. Direct blow with the point of an umbrella or stick thrust through the roof of the orbit or up the nose through the cubiform plate or by a violent blow on the chin or by gun shot wound through the roof of the mouth, may cause fracture of the base of the skull. The grave danger in all fractures of the skull apart from injury to the brain or concussion, is intracranial hæmorrhage from the rupture of one or both branches of the middle meningeal artery. The clot thus formed produces serious results by its pressure, on the brain. Pressure also results from depression of fragments of bone.

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\* Specially contributed to THE ANTISEPTIC.

(b) *Clean cut wounds* result from blows by a sharp cutting weapon such as a sword. They are not usually self inflicted. Insane persons and those bent on committing suicide may have recourse to such weapons.

(c) *Separation of cranial sutures* :—Occurs only in the young ; it is caused by a blow on the head with a blunt weapon and may occur alone but is often accompanied by fractures.

(d) *Perforation of bone* :—Is caused by bullet wounds resulting from projectiles discharged from firearms. There are usually two wounds in such cases, one at the entrance and the other at the exit of the bullet. The exit wound will be absent when the bullet gets lodged in the brain.

III. Brain.—Brain substance may be injured by cuts inflicted by sword, by laceration caused by depressed fragments of bone, by gun shot and other penetrating wounds. Contusion or laceration may occur without visible injury to the skull. It may occur from a fall or blow on the head on the same side or on the opposite side by *contre coup*. There may be no accompanying fracture of the skull. Concussion or brain-shock may be caused by direct violence on the vertex, by a violent fall upon the feet from a height or by an unexpected fall on the ground, when pushed down by a running cart or bicycle.

*Compression of the brain* results from a depressed fracture of the skull bone pressing on the brain or from intracranial hæmorrhage. It may also occur from the pressure of inflammatory exudation or pus on the brain tissue.

*Cerebral irritation* is the second stage of a brain injury. The patient is irritable in mind and body and remains more or less in a flexed attitude with slow pulse, low temperature, closed eyes and contracted pupils. Excreta is often passed on bed but the bladder may occasionally need to be emptied by a catheter.

**TREATMENT** :—The treatment of skull and brain injuries are the same, as any injury to the former affects also the latter. In all cases of brain injuries the first thing to do is to combat 'shock'. The patient should be kept in bed on the floor of a darkened room without a pillow to the head and the bowels kept well open either by the administration of drugs like calomel, croton oil or by a glycerine enema every other day. Unnecessary stimulation should be avoided for fear of inducing hæmorrhage. Diet must be restricted, milk and glucose in small doses should be given by spoon feeds. In a mild case of simple concussion there may be only unconsciousness for a time followed by rapid recovery. In more serious cases when unconsciousness is prolonged with a slowing of the pulse and no sign of fracture of the cranium, lumbar puncture may be done to relieve intracranial pressure. The immediate administration of 50% glucose intravenously, complete spinal drainage (removal of 45 to

100 c.c. of C.S.F.), restriction of fluid intake to 20 to 30 ozs. for the first 10 days and 32 ounces for the next 3 months, a daily lumbar puncture with abstraction of 45 to 60 c.c. of fluid constitute the treatment. This treatment is atleast logical in its thoroughness, but there is increasing doubt as to whether dehydration is necessary and proper and is at all desirable. High intracranial pressure may exist sometimes but is scarcely the dominant factor that makes the difference between recovery and death. Definite demonstrable neural damage is the common cause of symptoms of head injury (excluding concussion) and is the most potent cause of death. Oedema may contribute to death and so should be treated. Compression must be treated as if it was always present. The best method is to treat the patient primarily for shock and to apply other methods of treatment such as diagnostic lumbar punctures with pressure readings by a spinal manometer, intravenous hypertonic therapy when indicated and operation for hæmorrhages either extra or intradural and removal of depressed fragments of bones. There is little doubt that intravenous therapy is a safer method of treatment than lumbar drainage, as it recalls the fluid into even circulation. A retention enema of 4 ozs. of 50% magnesium sulphate may be used as a routine as it is not powerful enough to lower dangerously an intra-cranial pressure which does not need lowering. Dehydration has a place in the treatment of head injuries *after* the first 24 hours, for it is not a life-saving measure. It certainly fails to rouse the stuporous patient back to consciousness, which demonstrates, convincingly enough that this state is due to parenchymal damage and not to the water logging of otherwise normal tissues. But in the stages of recovery, dehydration is valuable particularly in restless patients and in those with severe headache. The judicious use of chloral, bromides, and morphia to prevent exhaustion are very helpful but the effects of one dose must be allowed to wear off before another is given.

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- |  |                                |
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#### Loss of Hair after Delivery

The fact that women lose hair excessively following pregnancy is a normal phenomenon. The increase of oestrogen during pregnancy usually leads to increased growth of tissues of ectodermal origin (skin, hair, sweat glands and sebaceous glands) and also to increased output of these tissues i.e., increased sweating, increased sebaceous secretion, and increased cervical mucus. It seems only natural, that following a drop in the blood level of this hormone after delivery, these functions should diminish and they do.—(*J. Am. Med. Assoc.*, 150:4, p. 434, 1952).

## PHOTOTHERMAL RADIATIONS— INFRA RED RAYS\*

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**Source.**—A spectrum is “a charted band of wave-lengths of electromagnetic radiations obtained by refraction or diffraction by means of a prism.” Each colour corresponds to a different kind of radiation. The rays beyond the red end are called “Infra-red-rays” and their heat can be recorded by a thermocouple. It was William Herschel of Germany who utilised these rays as a source of therapeutic heat. Tyndall of England demonstrated the convertibility of luminous rays to heat waves, with a penetrating effect upon the body. The Swedish physicist Angstrom was the first to measure wave-lengths. An Angstrom Unit is  $1/10,000,000$  m.m. or  $1/10$  millimicron. There are long wave infra-red-rays (15,000 to 120,000 A.U.) and short-wave infra-red-rays (7000 to 15,000 A.U.). The wave-lengths of infra-red-rays in general are graded between 150,000 to 77,000 A.U. The long-waves penetrate the superficial layers (0.5 m.m.) and the short-waves the deeper layers of the skin (5 to 10 m.m.) and act upon blood vessels, lymphatics, nerve-endings and the subcutaneous tissues. In general the infra-red-rays with thermal radiations are often employed for immediate local action.

**Forms of therapeutic heat.**—Heat for treatment purposes may be derived from many sources. Conductive and convective sources of heat are from hot water bottles, poultices, sand bags etc. which are popular home-remedies. Paraffin-baths and whirlpool baths, are more efficient sources of applying local heat. Radiant sources consist of heat lamps and infra-red heating units. The apparatus should be simple and easy to operate.

**Skin:**—The human body consists of a composite mass of tissues and fluids with varying electric conductivities. Skin resistance is of primary importance in electro-therapy. The skin may be considered a partial conductor, the conductivity of which is increased by mechanical, thermal and chemical stimuli. The skin varies in thickness in different regions of the body, from about  $\frac{1}{2}$  to 4 millimeters. Heat decreases skin resistance by perspiration caused by increased activity of the sweat glands.

“Every beat of the heart, every twitch of a muscle, every stage of secretion of a gland is associated in some way with electrical changes” (Starling). The skin is not merely a protective covering of the human body, but is also a complex structure engaged in the acts of respiration, absorption and excretion. Nearly all physical measures which are non-specific, are applied through the skin.

**Infra-red-radiators.**—Infra-red-rays are artificially produced by heating metallic conductors, on passing an electric current

\* Specially contributed to THE ANTISEPTIC

through them. The apparatus consists of a heating element which is mounted in the centre of a parabolic reflector, and warmed by an electric current to a dull red heat. The heating element consists of either a resistance wire wound or embedded on a non-conducting material or a rod or circular plate of resistant metal carborundum. There are small or large size radiators in the market, drawing 50 to 500 watts.

**Technique of application.**—The patient should be placed comfortably in a relaxed position and the part to be exposed brought directly under the apparatus so as to ensure good radiation. Usually the average distance of the apparatus to the part exposed is from 2 to 3 feet, depending on the sensitivity of the part and the intensity of the radiations and the type of reflector. The length of the exposure is from 10 to 15 minutes extending gradually up to  $\frac{1}{2}$  to 2 hours according to requirements.

**PRECAUTIONS:**—(1) If the patient complains of irritation, burning and discomfort the apparatus should be raised a few inches above the part, at which the patient feels comfortable. (2) In patients with peripheral nerve injuries, infra-red-radiations should be given with great caution so as to avoid blistering. No form of heat should be applied, beyond the limits of comfortable tolerance. The average maximum tolerance is  $113.9^{\circ}\text{F.}$  on the surface and  $117.8^{\circ}\text{F.}$  on the under surface. For every rise of  $100^{\circ}\text{F.}$  the rate of oxidation is increased 2.5 times. (3) Repeated exposures to infra-red rays may lead to a permanent pigmentation of the skin resembling the mottling on the surface of marble. Excessive infra-red radiations first cause a wheel of erythema and local oedema and later blistering. Careless exposures cause deep sloughing of the skin and the adjacent subcutaneous and fibrous tissues.

Infra-red radiations speed up recovery by early repair of the diseased tissues, promote relief of pain and establishment of the normal functions of the body.

**ADVANTAGES:**—Heat radiation, unlike hot water bottles, poultices etc., acts over a greater depth, without undue pressure, but under constant observation. These physical measures are not habit-forming, are very simple and also cheap enough for all patients, poor and rich.

**Physiological effects of heating.**—The application of infra-red-rays causes the skin to get hot immediately and the body to have a rise in temperature at the site of the exposure. The degree of rise is proportional to the source of heating and the intensity and the length of the application. The body with its heat-regulating mechanism tries to maintain a constant temperature. The vasomotor mechanism, then brings about a vasodilatation of the capillaries and stimulates the arterial and venous circulations. This local hyperæmia helps in the rapid collection and removal of waste products and increases phagocytosis.

The sedative effect produced by the heat through the sensory and motor nerves, accounts for the relief of pain in cramps, sprains and spasms. The general effect is manifest in the more rapid circulation and an increased metabolic rate with its attendant beneficial effects. Due to an increased circulatory rate there is a marked lowering of blood pressure and a rapid pulse rate. For every degree of rise in the temperature, the pulse rate is increased by about 10 beats. The luminous sources of infra-red-rays have a penetrating property and cause sweating from the subcutaneous glands in the area under exposure.

**Clinical uses of infra-red-rays.**—Infra-red-rays are a valuable adjunct to general therapeutic measures in the treatment of diseases, chiefly due to their mild heating action and their pain relieving properties. Radiant heat helps other physical measures like massage by rendering the tissues supple for manipulation. To improve skin conductivity, a few minutes' exposure to radiant heat should precede long-wave-diathermy and ultra-violet irradiation from mercury vapour lamps.

They are useful in treating folliculitis, furunculosis, and early cases of abscess formation obviating surgical intervention altogether. They are useful also in cases of peripheral circulatory diseases, like thrombophlebitis, endarteritis, Raynaud's disease, and in thromboangiitis obliterans. The heat should be maintained at about 97°F. to avoid complications. They are useful in catarrhal conditions of the mucous membranes in inaccessible locations *e.g.*, conjunctivitis, sinusitis and coryza and are particularly valuable in affording relief of pain in arthritis, neuritis, neuralgia, also in traumatic and inflammatory conditions, *e.g.*, continuous muscle strains, traumatic synovitis, sprains.

The radiations are helpful in maintaining the temperature of antiseptic dressings in infections and cellulitis.

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## Cases and Comments

### A CASE OF COOLEY'S ANÆMIA

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AND

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**Case sheet.**—A patient X, aged nine, the daughter of a Muslim medical practitioner of Madurai, fourth child and second daughter of the parents born in January 1943 was referred to the X-ray department on the 24th February 1953, for X-ray of the skull.

**Leading symptoms:**—Breathlessness on exertion, palpitation and general weakness since her fourth year and a prominent protuberance on the skull in the forehead region, since her second year.

**History:**—Symptoms developed insidiously and the father noticed a slight prominence on the right side of the forehead at the beginning of her second year which became more prominently noticeable by the beginning of 1948. A slight prominence of the abdomen was also noticed along with this. The girl developed breathlessness on the slightest exertion and sometimes also palpitation associated with a dull ache in the chest. Her appetite was good. Vague pains in the limbs troubled the patient to such an extent that she preferred to be reading some book or other instead of showing an inclination to play games at school; in the house she has acquired a proverbial good name for not getting entangled in any mischief as the other children of the house did. As regards her previous health, she is stated to have had no major illness since her birth.

**Personal and family history.**—Diet non-vegetarian. Parents are quite well as also the other children. The eldest daughter had hæmangioma on the right shoulder which has healed completely now.

**Physical examination:**—The general condition:—The patient has prominent zygomas which make the cheek bones stand out and has a face with mongoloid features. The patient looks undersized for her age and poorly nourished even though she comes of an average middle class family. Conjunctivæ, palate, and finger nails appeared pale. There was no jaundice. Cyanosis was not evident. The fingers did not show any clubbing. The skin was sallow, yellow. There was no enlargement of the lymph nodes nor œdema of the extremities. Teeth and tongue were clean, moist and the throat normal. The most striking points which were noticed, when one saw the girl, were:—the shape of the forehead, a prominent abdomen, and the marked intelligence of the child.

*Respiratory system* :—There were no anomalies noticeable in the form or movements of the chest.

*Abdomen* :—The liver was just palpable and the spleen was enlarged two-finger-breadths below the costal margin. No rigidity or tenderness or lumps detected in the abdomen.

*Nervous system* :—Sleep normal; on examination the intelligence, memory, mental powers and speech were found to be normal. The cranial nerves were normal. The spinal nerve functions sensory and motor were found to be normal.

*Cardio-vascular system* :—Pulse-100; regular in rhythm, soft, of small volume. Vessels soft and supple. Blood pressure; systolic-100; diastolic 60. Apex beat was visualised internal to the nipple, in the fifth intercostal space and confirmed by palpation. Systolic murmur (haemic in nature) was heard in all areas and most markedly in the pulmonary area. The patient's exercise-tolerance was poor.

*Investigations*.—Blood Hb.—46% (6.5 gm) calculated Sahli's scale—100% is equal to 14.8 gm. per cent. Total R.B.C. 2.9 million per c.m.m. Total W.B.C. 8,000 per c.m.m. Differential count: Polymorphs—58%. Lymphocytes—35%. Eosinophil—6%. Basophil—1.0%. Reticulocytes—6%. Peripheral blood picture as revealed by blood slide-erythrocytic picture-moderate anisocytosis and macrocytosis and poikilocytosis. Fragility of R.B.C. Lysis starts at 0.3% solution and complete at 0.25% solution. Icterus index 20 units. Volume index 0.90. Colour index was one. Mean corpuscular volume expressed in cubic microns 83.6; Mean corpuscular Hb. expressed in micro-micrograms 29.2. Sternal marrow: revealed nothing abnormal except the presence of premature cells of both the red and white cell series.

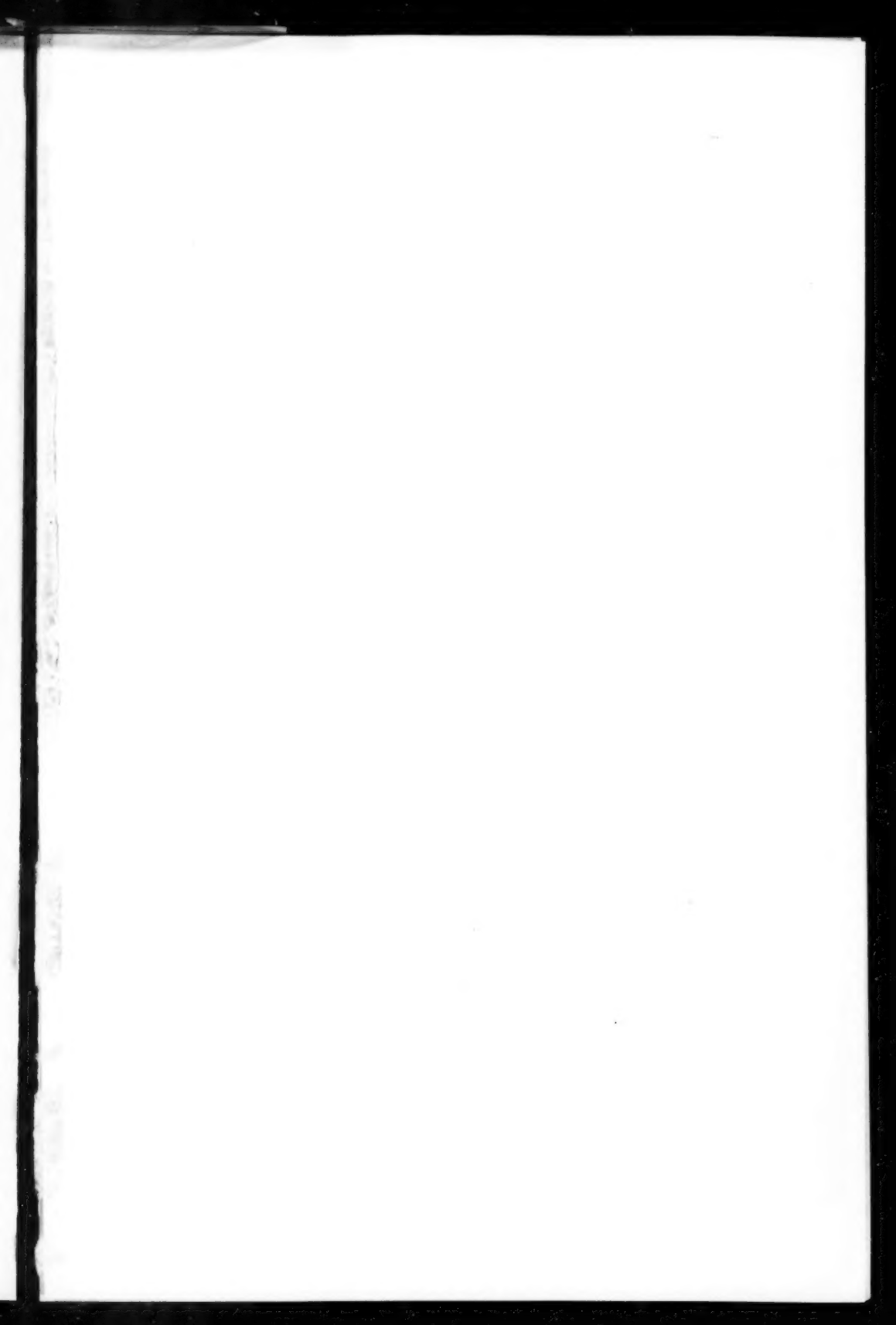
Blood :—Kahn: negative; Van den Bergh reaction—Direct—immediately positive.

Blood proteins: 6.3 gms. per 100 cc. of blood. Urine: smoky in colour, acid in reaction, sugar and albumen-nil.

Urobilinogen—Bile-salts, bile pigments—nil. Microscopic deposit full of R.B.Cs. and one to two pus cells. Motion: no ova or cyst.

*X-ray* :—Long bones :—shafts of the long bones are osteoporotic and appear to be swollen. Cortex is thinned by internal absorption. Entire skeleton is affected but the changes are most conspicuous in the long bones which normally have deep concave external contours such as metacarpals and femurs.

*Explanation for the changes observed in bones* :—Abnormal cells of both white and red corpuscles circulating in the blood stream, are destroyed prematurely by the reticulo-endothelial tissues; anaemia and haemolytic jaundice result. The bone-marrow in trying to compensate for the blood destruction proliferates excessively



A Case of Cooley's Anemia  
*M. G. Varadarajam and K. Radhakrishnan*



FIG. 1



FIG. 2



FIG. 3

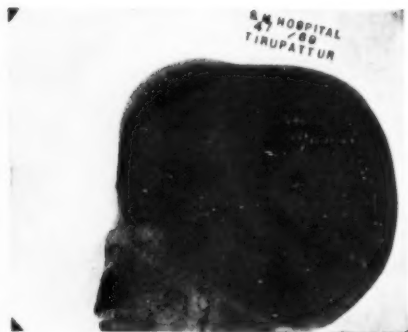


FIG. 4



FIG. 5



FIG. 6

FIGS. 1 & 2 — Note the prominence involving the forehead.

FIG. 3 — Skiagram of hand shows trabeculated osteoporosis and cortical atrophy.

FIG. 4. — Skiagram of skull shows widening of diploic space and atrophy of outer table with radial striations at right angles to the inner table.

FIG. 5. — Skiagram of lateral view of skull shows increasing atrophy of the outer table. Note the fuzzy outline of skull due to spicules of diploic bone being arranged in a radial pattern.

FIG. 6. — Skiagram of the pelvis and upper ends of femur which also clearly show the osteoporotic condition of the bones with medullary cavities appearing dilated.

and hypertrophies. The compensatory over-growth of the marrow within expansile young bones, causes dilatation of the medullary cavities and pressure atrophy of the spongiosa and corticalis.

*Hand*:—Tubular bones of the hands are optimal sites for the demonstration of skeletal changes. Normally bilaterally concave hour-glass-shaped metacarpals are swollen. The trabeculated osteoporosis and cortical atrophy are clearly brought out. Maturation is retarded.

*Upper extremity*:—Medullary cavities appear to be dilated. Shafts are swollen, and rectangular in outline and cortex is thin. All the bones are osteoporotic and present a trabeculated appearance owing to irregular destruction of the spongiosa and irregular internal erosion of the cortex. Similar changes are seen but less marked in bones of the lower extremities.

*Skull*:—A widening of the diploic space and atrophy of the outer table. (lateral view of skull taken on 12-12-'47) with radial striation at right angles to the inner table and spicules of diploic bones arranged in a radial pattern with their long axes extending across widened diploic space. This is most marked in frontal bone.

*Lateral view of skull taken on 24-2-'53*:—Widening of diploic space with displacement of outer table which has become mostly atrophic is noted. There is a peculiar fuzzy outline of the skull due to spicules of diploic bone being arranged in a radial pattern giving rise to an appearance often compared to the hair standing on end. Radial arrangement of diploic spongiosa is probably a compensatory phenomenon to support diploic space in the presence of a weakened atrophic outer table. Widening of diploic space, the absence of outer table and generalised radial striation, the last two features are supposed to be present in less than 20 per cent of cases.

*A.P. view of skull taken on 24-2-'53*:—Maxillary sinus is obliterated. Air spaces in the temporal bones and paranasal sinuses are encroached upon. Swellings of the zygomas are present—(owing to marrow hyperplasia and internal swelling of the temporal, paranasal bones, the air-spaces in the temporal bones and in the paranasal sinuses are encroached upon and sometimes obliterated. Swellings of the zygomas make the cheek bones stand out and are thus responsible for the mongoloid features seen in this case).

**DIFFERENTIAL DIAGNOSIS.**—Interest is usually centred on (1) the peculiar appearance of the face and the shape of the skull. (2) The splenomegaly with a palpable liver. (3) Anæmia. (4) Röntgenological appearance of the long bones and skull.

What first strikes one are the three principal chronic hæmolytic anæmias of infancy and childhood; viz., (1) Cooley's anæmia; (2) sickle-celled anæmia; and (3) acholuric jaundice or congenital hæmolytic anæmia or spherocytic anæmia. The other diseases are: (1) nutritional anæmia; (2) anæmia due to infection; (3) infantile

scurvy; (4) Von Jaksch's syndrome; (5) erythroblastic anæmia; (6) hæmorrhagic diseases of the new-born; (7) Lederer's anæmia and (8) leukæmia.

*Acholuric jaundice*:—A chronic familial disease characterised by crises of excessive blood destruction, a constantly high percentage of circulating reticulocytes, splenomegaly, spherocytosis, fragility of the red cells, and a variable amount of jaundice but no bilirubin in the urine. This is readily excluded by a fragility test. In this disease, the cells begin to hæmolyse at 0·75 per cent and the process is complete at 0·4 per cent.

*Sickle-cell anaemia*:—A severe hemolytic anæmia occurring almost entirely in negroes in which the red cells show a peculiar sickle shape under certain conditions. The disease is characterised by remissions and exacerbations of anæmia which are associated with abdominal and joint-pains together with a tendency to ulceration of the legs. This disease can be excluded by the absence of sickle-shaped red blood corpuscles in fresh blood preparations.

The three diseases mentioned above have a common pathologic mechanism—abnormal erythrocytes are generated by blood-forming organs—normoblasts and megaloblasts in Cooley's anæmia, sickle-cells in sickle-cell anæmia and spherocytes in spherocytic anæmia. Significant changes in tubular bones are rarely demonstrable in infants and children who suffer from sickle-cell anæmia. Cranial changes similar to those of erythroblastic anæmia have been found in many cases. Apparently, marrow-hyperplasia in long bones is much less marked than in Cooley's anæmia and for this reason bony changes secondary to overgrowth of the marrow fail to develop. In acholuric jaundice, skeletal changes however, are absent in most cases and when present are not striking and are variable. Cranial changes are more marked than those in long bones. Bony changes are more common in Cooley's anæmia than in the other two diseases.

Leuco-erythroblastic anæmia found in association with Cooley's anæmia is characterised by the presence in the peripheral blood of unusually immature cells of the red and white series and is found in association in certain diseases of bone and bone-marrow. The colour index is commonly below unity and the mean diameter of the cells are within normal limits. Reticulocytes are constantly above normal and nucleated cells are present in large numbers. The leucocytic count shows an excess of myelocytes and myeloblasts may be present.

The platelet count is low. Van den Bergh reaction is usually negative. Anæmia is presumably due to irritation or disturbance in the maturation of the hæmopoietic tissues by the bony disease. Anæmia is not hemolytic in origin nor does it seem to arise from destruction of hæmopoietic marrow. The ætiology of this condition is obscure. This blood picture is common in marble-bone-disease

of Alberg-Scoenberg which is a congenital disease, symptoms of which usually begin in childhood with fractures following trivial injury and characterised by increased density of bones, splenomegaly, and anæmia. The X-ray appearances are pathognomonic. Hodgkin's disease can be very easily excluded on other grounds.

**DIAGNOSIS:**—The case appears to be most probably a case of Cooley's anæmia. This condition described by Cooley in 1927, is a familial disease found in children of Mediterranean stock, known in Greece since 1910. Surprisingly enough the disease has not been identified in the Spaniards or in the Mediterranean French. However, authentic cases have now been described in Chinese and Asiatic Indian children. It is a disease of the Mediterranean races most often in Greeks, but also in Italians, Armenians and Sicilians. It is characterised by a constant familial and racial incidence, a typical facial appearance, distinctive changes in the bones and enlargement of the spleen. It usually appears in the first two years of life and sometimes in the new-born. It has been reported in identical twins. The skin is yellow, the face mongoloid, the head enlarged, the abdomen prominent and the stature stunted. The exact mechanism of inheritance is not well understood. There is now substantial evidence that the condition is hereditary and is transmitted to the offspring by parents with a benign latent form of the disease.

In conclusion, the above case appears to be a well established one of Cooley's anæmia although the precise nature of its inheritance is not understood.

**PROGNOSIS:**—The general outlook is not good, though, it is stated that after maturity it is better.

**TREATMENT:**—There is no satisfactory specific treatment available now. It does not respond to iron or liver therapy. There are varying opinions about splenectomy. The disease is slowly and progressively fatal. Most cases fail to reach the age of ten. None of Cooley's cases lived more than ten years. The only hope now offered is blood transfusion, the frequency of which depends on the percentage of hæmoglobin and the total red blood cell count. The case has to be carefully and regularly followed before any definite prognosis can be given.

Our grateful thanks are due to Dr. Muhammad Ismail Sahib, M.B., B.S., D.T.M., Superintendent, Erskine Hospital, Madurai, for his helpful suggestions and for permitting us to report this case and to Dr. Abdul Sattar, Ophthalmologist, Erskine Hospital, Madurai, for supplying us case-notes and investigations and also to the staff of the Erskine Hospital for their unstinted cooperation.

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## AN UNCOMMON TYPE OF URTICARIA

DR. MANORANJAN DUTTA,

*Medical Officer, New Savan Sugar Factory, Siwan, Bihar.*

ON 16-1-'53, I was asked to see, M. R., a Hindu lady, aged 25 years, well-built, mother of three children, the youngest being one year old. There was nothing important as regards past history.

History of present attack (as described by her husband):— On 9-1-'53 at about 8 a.m. she suddenly developed a severe itching sensation all over the body followed soon after by the appearance of large urticarial rashes. As a result the patient being fair in complexion turned almost red, remained drowsy, and passed urine involuntarily. This stage lasted upto 5 p.m. after which the rashes slowly disappeared and by about 9 p.m. she became free from the trouble; she remained free, on the next day also. But on the day following (11-1-'53) she developed all the symptoms of the first day with the same duration, type and severity. She had four similar attacks on every alternate day i.e., on the 9th, 11th, 13th and 15th Jan. She remained quite free in the intervening days.

Examination.—On examining the patient I found the patient to be symptom-free; she complained only of slight headaches and weakness. She simply corroborated her husband's narrations, and said she had no such attacks previously. Her monthly periods were normal. Pulse 78; respiration 20 per minute. Temperature  $97.5^{\circ}\text{C}$  in the axilla. Heart, lungs and liver showed nothing abnormal. The spleen was slightly enlarged, tender and soft. No abnormality could be detected in the pelvic cavity on palpation. The skin was dry, lustreless, rough and felt tender even to mild pinching. No septic focus could be detected.

She had been seen and treated by other doctors during her previous attacks:—On 9-1-'53—She was given a mixture containing Sodii citras gr. 15, Pot. citras gr. 15. Pot. bromide gr. 10, per ounce, one dose to be taken every 4 hours; and powders containing Ephedrin hydrochloride gr.  $\frac{1}{2}$ , Cal. gluconate gr. 60 divided into 3 powders, one given every 4 hours. On 10-1-'53, the same were repeated and on 11-1-'53, she was given a mixture containing Pot. brom. gr. 10, Sodi citras gr. 20, Pot citras gr. 20, Hexamine gr. 10, per ounce one dose every 4 hours, and powders containing Ephedrin hydrochlor gr.  $\frac{1}{2}$ , Antistine 3 tablets, Cal. gluconate gr. 60, Celin 50 mg. T6 Gardenal gr.  $1\frac{1}{2}$ ; divided into 3 powders and one given every 4 hours; she was also given Lacto-protein 5 c.c. intramuscularly at 10 a.m. and Calcium with vitamin C (Sandoz) 10 c.c., slowly by the intravenous route. On 12-1-'53, the treatment was the same as on 11-1-'53 with the addition of warm-alkaline sponging of the whole body and an opening dose of Mag. sulph in the morning.

On 13-1-'53, (1) Repeat mixture. (2) Ephedrin hydrochlor

gr.  $\frac{3}{4}$ , Osto-calcium 4 tablets, Celin 50 mg. 6 tabs. divided into 3 powders one to be taken after each dose of mixture. (3) Anthisan 2 c.c. (one amp.) by subcutaneous injection at 8 a.m. (4) Cal. with Vitamin C 10 c.c. intravenously. (5) Crystalline penicillin sodium, 5 lacs units in 2 c.c. of redistilled water intramuscularly at 8 a.m. and Seclophen 1 vial in 2.5 c.c. of redistilled water at 12 noon. (6) Warm-alkaline sponging. The injection of milk-protein was stopped.

On 14-1-'53, the patient refused to take so many injections and so all the medicines which were to be taken orally were repeated with the addition of Anthisan 0.1 gm. tablet one thrice daily. Only Seclophen injection was continued, one vial in the morning and one in the evening.

On 15-1-'53, she received the first injection of Seclophen in the morning and at about 9 p.m. she again developed urticaria and other symptoms.

The patient refused to continue any longer under the attending doctor's professional care and treatment.

I was therefore called in and was amazed and really perplexed when I saw the treatment chart, which was shown to me. I set out to find the relation of this allergic attack to any particular food, or extraneous source likely to induce it; nothing suggestive could be detected. No obvious septic focus, was found nor a history of amoebiasis, or intestinal worms; she had in fact taken no medicine whatever, for a long time prior to this attack.

By careful questioning it was ascertained that during the attack, her skin temperature was raised to as much as 101°F to 102°F as judged by the sense of touch though the temperature was not actually taken and recorded.

It therefore occurred to me that the urticaria may be related in some way to this rise in temperature and that the tertian periodicity of the rise in temperature was probably due to malaria; this was to some extent corroborated by the enlarged, soft and tender spleen. The liberation of a pyrogenic substance apparently gave rise to the peculiar allergic manifestation, which was obviously therefore, a type of "haemoclastic shock."

I promptly gave an intra-muscular injection of Quinacrine soluble, 300 mg. in 3 c.c., of redistilled water at 12 noon and prescribed Camoquine 3 tablets, one to be given every three hours and awaited a report from the relatives on the next day when an attack was due, on the basis of the previous ones.

But she did not get it and I prescribed one drachm of Liquid alkacitron in an ounce of water, every four hours and one tablet of Paludrin 0.1 g. to be taken after each dose of the mixture.

The patient was cured by this treatment. So therapeutically the diagnosis was confirmed that the urticaria in this case was an allergic manifestation of malaria. An interesting point is that she was living in a malarious place and had had attacks of malaria previously but without any allergic manifestations such as were noticed on the present occasion.

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#### **Prevention of Monilial Complications due to Antibiotic Therapy**

Oral undecylinic acid apparently prevents the so-called monilial complications which occur with the broad-spectrum antibiotics in a high percentage of patients to whom it was administered prophylactically by Drs. D. C. Mountain and F. P. Krumenacher of the Columbia Hospital (*Am. J. Med. Sci.*, Mar. 1953). None of the patients who were given simultaneously one of the broad-spectrum antibiotics and oral undecylinic acid developed pharyngitis, glossitis, pruritus ani, pruritus vulvæ, vaginitis, or proctitis.

Two out of 42 patients who received undecylinic acid three days after the antibiotic was started developed pruritus ani. This is a failure in only 3.2 per cent of the total number of cases in which oral undecylinic acid was used. 12 out of the 45 control cases developed one or more of the above symptoms (26.7 per cent). There were no side reactions to oral undecylinic acid nor did it interfere with the clinical effectiveness of the antibiotic used, since a high percentage of the patients made very good recoveries, from their various infections.

The oral use of undecylinic acid should be considered whenever oral aureomycin, chloramphenicol, or terramycin is administered. The authors suggest that one capsule (0.44 g.) of the drug be given simultaneously with each 250 mg. of the selected antibiotic. Undecylinic acid does not however, prevent the diarrhoeas which occur secondarily to these antibiotics, nor does it inhibit the growth of the proteus pseudomonas or hæmolytic staph. aureus.—(*Cur. Med. Dig.*, June 1953, 20: 6, 115-116 and *Intern. Med. Dig.*, June 1953).

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#### **ACTH: Cortisone and Tuberculosis**

Capon reports 2 cases in which ACTH and Cortisone acted adversely on tuberculous infection. In the first, tuberculous pus was aspirated from an axillary gland and from the shoulder joint after treatment of scleroderma and dermatomyositis with cortisone. In the second the patient who had disseminated lupus erythematosus, improved with cortisone, but then became very ill with miliary spread of tuberculosis through the lungs and to the meninges.—(*The Canadian Med. Assoc. Jour.*, July 1952—*Abst. Med. Jour. Austral.*, 13-12-1952).

## A CASE OF REITER'S SYNDROME

R. NATARAJAN, B.Sc., M.B., B.S.  
"Rathika", Kumbakonam.

THE following case is reported as representing a somewhat unusual manifestation of physical findings, known by the name of Reiter's syndrome. The patient is Mr. D., Hindu, male, 48 years old, a motor driver by profession. Following a venereal exposure 2 months back, he developed urethritis for which he took immediate treatment with penicillin in a local hospital. The urethritis did not respond to the treatment and he developed burning pain during micturition. Fifteen days later, he developed pain in the back. Then, the right ankle, both the knees, the left shoulder, the right metacarpo-phalangeal joints became involved causing considerable pain in those joints. The right ankle joint is actually swollen and movements are limited, due to the swelling and pain. The joint pains are migratory in nature. Ten days back, he developed conjunctivitis of both eyes with a slight mucoid discharge. Nothing abnormal was detected in the other systems and there were no skin lesions.

INVESTIGATIONS :—The urethral discharge was negative for gonococci. Total W.B.C. 10200 c.m.m. Differential count: P. 82. L. 10. E. 7. M. 1. The sedimentation rate was 52 mm. in one hour. Joint biopsy, cultures, and complement fixation tests were not done owing to lack of facilities.

TREATMENT :—The patient was given a full dose of penicillin for three days and was given massive doses of salicylates; he is now being treated with Irgapyrin tablets. He was given the usual treatment for the eye condition. His joint pains and conjunctivitis have not improved so far. Though the urethral discharge has become scanty, he is still having the burning pain during micturition. He is too poor to afford terramycin or corticotrophin.

COMMENT :—*Symptomatology* :—This syndrome was first described by the German physician, Hans Reiter in 1916, while he was serving in the army as a Lieutenant. It is indeed, a triad of symptoms: polyarthritis, non-specific urethritis, and conjunctivitis. Diarrhoea often precedes the urethritis. The diarrhoea is often mild and the patient may usually forget to mention it. Occasionally keratitis, iritis and iridocyclitis may also occur. Not infrequently cystitis, prostatitis and prostatic abscess have been noted. The involvement of joints is usually multiple and migratory. There is a predilection for certain skin lesions to appear over the affected joints especially in the lower extremities and over the scrotum and penis. Splenomegaly has rarely been noted.

*Aetiology* :—The definite cause of this disease has not been determined. Some investigators obtained high agglutination titres against dysentery and therefore, thought that those organisms might cause this disease. Others believe that the disease is due

to a group of 'L' organisms or the Pleuropneumonia organisms which have been found in the urethral discharge in many cases and very rarely in the joint exudates. Some consider that it is just like any gonococcal infection and may be followed by rheumatoid arthritis. The follow-up of cases of gonococcal arthritis has shown that many go on to typical rheumatoid arthritis. The prompt response of gonococcal arthritis to penicillin may help to eliminate gonococcal arthritis. The use of penicillin will be an important diagnostic aid.

The mode of entry of the organisms is also not clear. In cases in which diarrhoea is present, entrance through the digestive tract is likely. In cases with no diarrhoea, the probable entry is through the genital tract. While cases are mostly limited to men in the third and fourth decades of life, the disease may occur also in women.

*Pathology*:—Joint-biopsy usually reveals congested and purplish synovia. Microscopic examination shows intense inflammatory reactions limited to the superficial layers, not involving the supporting collagen, fibrous connective tissues or vessel-walls.

*TREATMENT*:—Many types of therapy have been tried including sulphonamides, penicillin, arsenicals, gold, and fever therapy, all without any effect. Some authors have reported notable improvement following the use of corticotrophin and they believe that Reiter's syndrome is not a separate entity but is only an allergic form of nonspecific polyarthritis. Willcox and Findlay have reported good clinical response in four cases of Reiter's syndrome treated with oral terramycin. Terramycin appears to be the antibiotic of choice for infections caused by pleuropneumonia-like organisms.

*Prognosis*:—Prognosis is good as regards life. Permanent ocular and joint involvements though unusual, may occur.

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The young physician starts life with twenty drugs for each disease and the old physician ends life with one drug for twenty diseases.

—Sir William Osler.

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A substantial reduction in cancer mortality is possible if the disease is detected in its early stages and treated without delay.

—(Statistical Bulletin, M.L.I. Co.)

## AUREOMYCIN IN THE TREATMENT OF TROPICAL EOSINOPHILIA

N. R. BANNERJEE, M.B., B.S. (Lko.), D.T.M. (Cal.),

*Specialist in Tropical, Skin Diseases and Leprosy,*

*Bati Chowk, Gorakhpur.*

THE only known treatment of tropical eosinophilia is arsenic in some form. But it does not effect a radical cure. Very often patients return with a recurrence of the same complaint and blood examination always reveals the same picture. The incidence of the disease is rapidly increasing from day to day. It is high time a permanent cure is discovered by means of sustained researches.

Many physicians have tried aureomycin; the results with aureomycin have been uncertain and adequate clinical data are not available yet. Aureomycin was tried because the aetiological factor was believed to be a virus.

I give below a report of 5 cases treated by me with aureomycin.

CASE 1.—Miss R.B., a young girl, aged 9 years, with cough, breathlessness, loss of appetite, gradual loss of weight. Physical findings revealed a few scattered rhonchi in both lung fields. Total W.B.C. count was 22,000 c.m.m. with 34% eosinophils. She was diagnosed as a case of tropical eosinophilia. This was her first attack. She was put on aureomycin, 50 mg. every six hours for 8 days. Clinical examination found her very fit after 8 days. The blood was re-examined after a fortnight. Eosinophils were 15% and the total count was 12,000 c.m.m. Though the blood count was still high she was clinically not a patient. Blood count reached normal after another fortnight i.e., one month after commencing the treatment. Eosinophils became 5% with a total count of 8,650 c.m.m.

CASE 2.—N. K., aged 4 years with a dry irritating cough and breathlessness for the last one month without responding to cough mixtures. Blood examination showed eosinophils 24%; total count 24,100 c.m.m. He was put on aureomycin, every 50 mg. 6 hours for 8 days. Improvement was marvellous clinically and pathologically.

CASE 3.—Mr. S. D. T., aged 29 years, gave a history of tropical eosinophilia. He had 4 relapses, one every 6 months, and was getting acetylsan, mapharside and also NAB. This was his 4th relapse. I put him on aureomycin 250 mg. every six hours for 8 days. Clinically he became all right after just one week. To start with, his count was 46% eosinophils with a total count of 30,350 c.m.m. After the completion of treatment, eosinophils had decreased to 11% and the total count 10,700 c.m.m.

CASE 4.—Mr. V. B., aged 26 years, came to me a year ago complaining of a dry hacking cough, pain in the sternal region, fever, palpitation and breathlessness and loss of appetite. There was a family history of tuberculosis. He was sent for X-ray which showed uniform mottling and cotton-wool appearance of both

lung-fields and accentuation of para-bronchial markings. Eosinophils were 49% ; total count 23,100 c.m.m. He was given a course of acetylarsan. Clinically he was all right after only 4 injections. He took 10 injections in all with gradually increasing doses. After exactly one year, he returned with the same complaints. It was quite apparent that it was a relapse and eosinophils were found to be again 46% with a total count of 21,650 c.m.m. He was put on aureomycin, 250 mg. every six hours for eight days. There was absolutely no change in his condition. Blood was re-examined. Eosinophils were 36% with a total of 20,800 c.m.m. Aureomycin induced no response in this case. He was therefore, again given acetylarsan, on which he gradually improved and was soon all right.

CASE 5.—B.S.G., 27 years, healthy. Complained of breathlessness, palpitation, dry cough, slight temperature (99°F—100°F) particularly in the evening and hæmoptysis. Blood examination showed eosinophils 22% ; total count 20,050 c.m.m. He gave a previous history of this disease and this was his 5th relapse in 2½ years. He had tried all arsenicals, and had albuminuria also. I put him on aureomycin, 250 mg. every six hours for 8 days. There was absolutely no improvement though the eosinophil count came down to 17% with a total of 18,250 c.m.m. Sputum and the tuberculin test were negative.

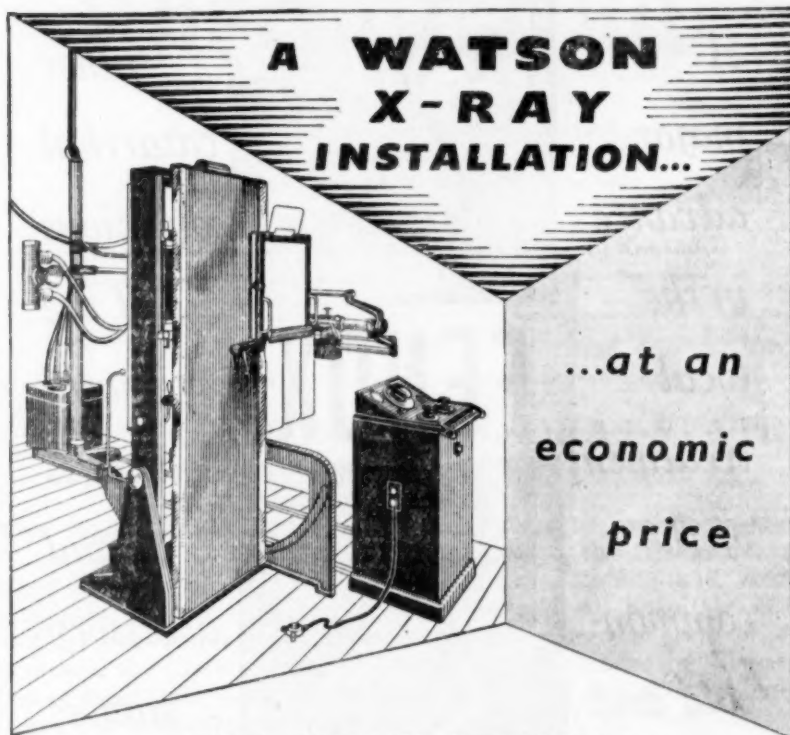
Conclusion.—The first three cases were followed for nearly two years with no relapse. The other two did not improve with aureomycin. Treatment of this disease with aureomycin is thus a gamble. Researches are in progress in many places in our country to know the ætiology of the condition. The experience of fellow practitioners on the use of aureomycin in this disease, will be interesting. The disease is a benign one and arsenic almost certainly cures it, atleast temporarily but patients with albuminuria are a problem.

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### *Eosinophilia*

The exact role of the eosinophil in physiologic and pathologic processes is unknown. There is generally an increase in the total eosinophil count in conditions associated with hypersensitive reactions such as those seen in allergic states and in parasitic infestation. Eosinophilia is also seen with certain destructive skin lesions, the "collagen" diseases, certain poisonings and some other conditions possibly related to foreign protein and sensitivity reactions. It is also a feature of certain blood and marrow disturbances.—(*N. Y. State Jour. Med.*, 15-7-'53).



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## OVERCROWDING IN MADRAS STATE HOSPITALS

THE Madras State Health Minister's replies to recent questions in the Madras Legislative Assembly about the Nellore District Head Quarters Hospital revealed that, under-staffing and under-equipment constituted a prominent feature of all hospitals in the State and that though improvement in these directions was urgently needed the Government was unable to find funds for construction of more buildings and providing more staff and greater amenities. The latest report on the working of the Civil Hospitals and Dispensaries in the State during 1951, which has just been published, confirms the Health Minister's observations. The deplorable overcrowding in the hospitals, will be seen from a few examples cited below:

In the Head Quarters Hospitals at Cuddalore and Bellary, there were on an average 280 and 348 in-patients, daily whereas the sanctioned accommodation was only for 140 and 152 respectively. This meant that an equal number or even more patients were lying on mats on the floor instead of on cots, and without suitable bedding, linen and crockery etc. At Chittoor, there were 159 in-patients for 95 beds and Ellore had 153 for 95 beds. The same was true also of Cuddappah. At Vellore, the daily average was 273 against a sanctioned strength of 153. Coimbatore, with its large industrial population had a daily average of 694 in-patients and only 366 beds. In the City of Madras, where there are three general and several specialist hospitals, the conditions are not better. The Stanley Hospital at Royapuram had during the year 1951 a daily in-patient strength of 804 with only 462 beds. This excessive overcrowding is particularly to be deplored in a

teaching hospital. Conditions at the Madras General and Royapettah Hospitals are much the same. It was only in the Vizagapatam Hospital that we find a daily average of 781 in-patients, for a bed strength of 700. The figures for 1952, and 1953, when the story comes to be told, would be very much higher, pointing to still more over-crowding.

This chronic state of over-crowding is in part at any rate, due to a sense of compassion and sympathy for human suffering, in the minds of the Superintendents. We do not wish to be uncharitable to the well-meaning Superintendents, by characterising their attitude as wrong or due to misplaced kindness. But it should not be forgotten that, by doing so, the staff is considerably overworked and their efficiency is greatly impaired. Government cannot by any means, look upon this state of affairs with equanimity or a sense of satisfaction. The report, under review, tells us that about one lakh and thirty four thousand more patients were admitted to the wards in the State hospitals in 1951, than in the previous year but that the Government increased the number of beds only by 342, and the staff and equipment only in proportion to this very small increase of bed-strength. Proposals for larger increases under these heads, put up by the officers of the Medical department, were turned down or ordered to lie over. The hospitals cannot therefore, afford to make more admissions, till more accommodation, staff and equipment are provided by Government.

The specialist hospitals in the City and Mofussil have also the same and perhaps a more pathetic tale to tell. Thus for instance, in a booklet entitled "Treatment of Mental Diseases in the Madras State" published by the Director of Information of the Madras Government, Dr. A. S. JOHNSON, the Superintendent of the Madras Mental Hospital refers to the newer methods of dealing with mental cases and deplures the lack of the essential facilities for undertaking in a proper manner these improved methods based on modern advances in psychiatry and psychotherapy. The care of the mentally ill patients has been reorganized in the Madras Mental Hospital since 1949 "by rearranging, and equipping the wards on the same lines as ordinary hospital wards placing them in the charge of medical officers for regular medical and psychiatric treatment. But the hospital has insufficient space for the various types of activities enjoined by modern science for the cure of mental diseases." The wards of all the three mental hospitals in the Madras State in Madras, Kozhicode and Waltair are over-crowded and under staffed. Thus there are only about 16 doctors and 40 nurses for over 2000 patients in the Mental Hospital in Madras for both night and day shifts together.

It is needless to say that this provision is wholly inadequate, and that the staff are considerably overworked. The admission under these conditions, of more patients than the sanctioned

bed-strength of any hospital is obviously wrong and will result in overcrowding, inadequate attention by the staff, the necessity for rationing the diet and even the therapeutic remedial agents required for treatment. Further, there is bound to be a decline in the morale of hospital administration.

It is therefore, imperative at the present juncture that representative bodies like the Medical Council and Medical Associations the Nurses' Council and Nurses' Associations, should forcibly impress on the authorities, the urgent need to relieve overcrowding which causes great strain to the staff and often discomfort to patients.

Government on its part should increase the staff and equipment to meet the needs of atleast those admitted beyond the sanctioned strengths. One of our leading local contemporaries recently made a very pertinent suggestion in this connection which we consider worthy of consideration and adoption by the Madras State Government. "A part of its present over-subscribed loan might justly be devoted to meet this urgent need. Until all hospitals are adequately staffed and equipped to deal with the number of patients admitted, the Superintendents should refuse to admit more patients than there are beds. Such action may appear drastic but it will be in the best interests of patients and staff".

We have repeatedly stressed in these columns, during the last five years and more the urgent necessity for providing adequate medical relief to the people and for improving their health and physique by sanctioning more liberal grants, from State revenues. The Medical and Public Health budgets of all the States in India, receive year after year a stepmotherly treatment at the hands of the Budget framers. They unfortunately fail to realize, that all their schemes for improving the economic status of the people and their standards of living will materialise *only* if the health and physical well-being of the people are efficiently looked after and maintained at a high level. While we repeat our request to Governments to view the Medical and Public Health needs in a more practical and liberal spirit, we wish to suggest the desirability of utilising part of the present over-subscribed loan to advance this most laudable and humanitarian work.

## THE TUBERCULOSIS PROBLEM

(Treatment and Rehabilitation)

“TUBERCULOSIS, being a social disease, it should be the concern of every individual in the country to take up arms against it. I would appeal to those who can afford to spare both money and leisure to bear a larger share of the burden and provide a stimulus to others to associate themselves with this noble effort” said RAJKUMARI AMBIT KAUR, Union Health Minister while opening a

T.B. Hospital in Delhi on the 20th of July last. Excellent advice emphatically stated no doubt; for two and a half million people in India suffer from tuberculosis—and this is a modest estimate—and 50,00,000 die annually from it! The economic loss to the country is therefore, enormous. But the Central and State governments in India have consistently been pleading paucity of funds for health activities!! At present only one out of every 200 patients in India can get a bed in a T.B. Hospital and a large number of these are too poor to pay the cost of treatment even if they can find accommodation. The question of maintenance of their dependents and the education of their children, is yet another big problem, when the breadwinner is the victim of this disease. The future of those patients who are more or less cured and become fit enough to take up some kind of occupation, but are unable to get suitable opportunities for work, is yet another and more serious problem which intensifies the tragedy of the whole situation.

The BCG mass vaccination campaign which was started in three states in April 1951, has since been extended to all states, where it is making fairly steady progress, though a large proportion of the 17 crores of persons below 20 years of age, who need BCG vaccination still remain to be tackled.

Any anti-tuberculosis programme should really take into account not only the therapeutic side, but also the prophylactic and rehabilitation aspects as well. Better housing conditions, higher standards of living and education of the people regarding preventive measures are urgently needed. The people of the country, we are glad to say, are becoming more and more TB conscious. All non-official bodies should create the necessary atmosphere and stimulate public enthusiasm in dealing with the problem. "Any programme to cover the varied aspects of anti-tuberculosis measures in India on the basis of a 15-year-plan will cost about 500 crores of rupees, exclusive of social services which include the maintenance of patients in their homes as also of their dependents and the rehabilitation of suitable cases" said our Union Health Minister. Admittedly it is not possible for Government alone to initiate and carry out successfully, measures involving such heavy expenditure. Private munificence and charity should therefore, be tapped and non-official activities encouraged. We are glad to see that small scale institutions for specialised treatment of tuberculosis are slowly springing up as a result of private and public non-official charities in several places in the country. But these are few and totally inadequate to meet India's large demands.

The first annual report and the welcome address of the Chairman of the Board of Trustees of the Mahatma Gandhi Memorial Tuberculosis Sanatorium at Sengipatti in the Tanjore District which was opened on 9th December 1951 by the then Chief Minister of the Madras State, reveals the fact that this very large and well-

conducted institution which was *started straightaway with 160 beds*, came into existence almost entirely out of private charity and non-official public munificence to the tune of about 25 lakhs of rupees. We learn also that the Institution has since received endowments from leading philanthropic gentlemen of the District in the shape of rich and extensive cultivable lands yielding a large recurring annual income for the maintenance of a certain number of patients but not of all the 160. This institution serves then, as a fitting example and a model of what intensive non-official effort and the willing co-operation from an enlightened and discerning public can achieve in the direction of affording relief to tuberculosis patients. But as the Chairman of the Board of Trustees pointed out at the Anniversary meeting held on 13-4-1953 "in the absence of patronage from the Government, the private philanthropists may not be enthusiastic in continuing or extending their patronage to this Institution". We heartily commend this appeal of the Board of Trustees for patronage, to the notice of the State Government, to enable the Institution to expand its activities, so as to include rehabilitation and after-care of discharged patients.

Voluntary agencies should no doubt also come forward to supplement the activities of the government and non-government tuberculosis hospitals and sanatoria in the after-care of the patients. The war against tuberculosis has to be waged on many fronts. The rehabilitation or after-care of discharged patients is an important one. The ex-patient's colony consisting of 8 cottages at Amrit Nagar, Tambaram, was started in 1952 with the express object of providing adequate help to the patient and his family and seeing that neither he nor the family suffered hardship which could be prevented. A further addition of 7 cottages was made in May of this year and the colony of 15 cottages will now accommodate 45 single members. Light work for a few hours a day and medical supervision have been provided for the rehabilitated patients. The Madras Health Minister who opened the additional cottages expressed the wish that they should soon have such after-care colonies and also more sanatoria and hospitals for treating tuberculosis in various districts. We would only wish that the Governments both at the Centre and in the States translate their pious wishes and hopes into action by allotting adequate grants for such essential purposes. They should extend liberal financial help to all the existing institutions for expanding their activities and enlarging the scope of their usefulness. By doing so, they would certainly help and advance the cause of tuberculosis control at minimum cost to themselves, particularly when as now, they complain of a paucity of funds for subsidising health activities in adequate measure.

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### BENEFITS AND RISKS OF BUTAZOLIDIN (BTZ) THERAPY (A Review)

PHENYLBUTAZONE (Butazolidin-BTZ) is one of a group of pyrazole derivatives developed in an attempt to find compounds with pharmacological properties similar to aminopyrine but without its toxicity. Several clinical trials were conducted in Germany and Switzerland with a combination of amino-pyrene and phenylbutazone in equal parts (this mixture is known as Irgopyrine in Europe and Butapyrin in America). These studies were started as phenylbutazone was found to promote the solubility of the relatively insoluble aminopyrine, thus permitting its parenteral use. Kuzell and his co-workers of the Stanford University School of Medicine in San Francisco, carried out clinical trials with phenylbutazone on 140 patients with gout and a variety of other rheumatic disorders. They found that there was improvement in all the 48 cases of acute and chronic gout. A suppressive effect was noted in all cases of rheumatoid arthritis but there was a prompt return of the symptoms in less than a week after stopping the medication. Beneficial effect was noted also in ankylosing spondylitis, rheumatoid arthritis with psoriasis and rheumatoid arthritis with degenerative joint-disease. They observed also toxic manifestations which included rash, oedema, nausea, activation of peptic ulcer, vertigo and pain at the injection site. Currie in Britain (*Lancet*, 1952; 2:15) Stephens *et al* (*J.A.M.A.*, 150: 1084) and Steinbrocker *et al* (*J.A.M.A.*, 150: 1087, 15-11-'52) in U.S.A. reported essentially similar benefits in various types of arthritis. Steinbrocker *et al* found that 81 out of a total of 117 patients with rheumatoid arthritis achieved appreciable relief of pain and they also obtained good results in other types of arthritis including osteoarthritis and gout. Dr. Rhys Davies and his colleagues of the West Herts Group of Hospitals of Physical Medicine in London, presented at the end of last year, their observations on the use and toxicity of butazolidin in more than 70 cases of rheumatoid arthritis. They were able to record improvement which was impressive and at times dramatic. In only 2 cases, did it appear to be ineffective. It proved remarkably effective in relieving the pain of osteoarthritis.

The superiority claimed for Butazolidin in the treatment of rheumatism lies mainly in its being a potent analgesic. The discussion held on 10th June 1953 in the Section of Physical Medicine, during the general meeting of the Royal Society of Medicine in London, with Dr. Donald Wilson in the chair, centred round the value and limitations of Butazolidin as a therapeutic agent in arthritis. Several reputed physicians with wide experience in the treatment of rheumatic and allied conditions took part. All of them agreed on the superior analgesic property of the drug. Dr. John Shulman had no doubt that Butazolidin raised the pain threshold; and had an anti-inflammatory action, with an associated

effect on capillary permeability. The blood uric acid level was reduced in cases of gout. The most important side-actions were fluid and sodium retention and a toxic action on the bone-marrow. Dr. Rhys Davies who had had eighteen months' experience of phenylbutazone (BTZ) in treating 173 patients with rheumatoid arthritis, showed that the grading of severity was not significantly affected by treatment, but stated that he was impressed by the feeling of well-being induced in his cases by the relief of pain and by the accompanying functional improvement. Butazolidin afforded relief when other drugs had failed—an undoubtedly strong point in its favour. The results obtained by Dr. T. H. Howell in a clinical trial at Queen's Hospital, Croydon and in the Geriatric Research Unit at St. John's Hospital, Battersea, London, on patients with chronic rheumatoid arthritis, were encouraging. (*Med. World*, 5-12-1952).

At the annual meeting of the American Rheumatism Association held on 28th May '53 in New York, Kuzell of San Francisco reported further results he had obtained in the treatment with BTZ of another 800 patients suffering from a variety of rheumatic diseases. He found it an effective and useful, but a temporary suppressive agent. Patients with gout and ankylosing spondylitis showed the best response. Yeoman of Tucson had treated 40 patients with rheumatic spondylitis for periods up to 2 years and in his series the drug had to be discontinued in only one case because of toxic effects. Eleven had gone back to work and three became fit enough for surgery. The maintenance dose used by him was 200 mg. per day.

Nassen and Pilkington (*Br. Med. Jour.*, 14-6-1953) treated 109 patients suffering from various rheumatic conditions and found the drug useful and most effective in combating the symptoms of acute rheumatoid arthritis and gout. Its trial in chronic disabling conditions is justifiable since there are a number of patients who derive benefit without serious toxic manifestations. They consider that the scarcity in the supplies of ACTH and Cortisone is another factor in favour of using Butazolidin (BTZ). If used in doses not exceeding 0.4 g. every one to ten days, only transient rashes are likely to occur. Dr. Rhys Davies *et al* used 1 g. Butazolidin (BTZ) by intramuscular injection daily for 10 days, then every second day for ten days and every third day for three further injections. The outer aspect of the thigh and the upper outer quadrant of the gluteal region were the sites of injection. Their observations on the pharmacological findings agreed with those of Gsell *et al* (*Schwz. Med. Wschr.*, 80:310, 1950) who noted that BTZ attains high concentrations in the blood soon after the injection and falls over 48 hours to a low level which persists for still another 48 hours before finally disappearing. No cumulative effect was demonstrable, nor any increased clinical effect with larger doses

up to 2 g. daily. They gave BTZ also by mouth to over 150 patients starting with not more than 1 g. daily and reducing it to a maintenance dose of 800 mg. or less on alternate days. Kuzell *et al* administered BTZ orally in the form of coated tablets containing 125 or 200 mg. as well as intramuscularly in a 20 per cent solution of its sodium salt. The range of oral dosage was between one and six tablets a day. Injections were reserved for acute conditions in which the range was 0.6 g. to 1.0 g. once a day until relief of symptoms was obtained. Freeland and his co-workers of the Department of Physical Medicine in the London Hospital (*Lancet*, 20.6.1953) used 200 mg. of the drug for a dose, thrice a day, for 28 days. Currie (*Lancet*, ii, p. 15, 1952) and Davies *et al* (*B.M.J.*, 1952, ii, 1392) also gave 1 g. of BTZ daily for 10 days.

It is fairly obvious therefore, that many patients with musculoskeletal disorders derive great benefit and worth while relief from the use of BTZ. The question of the toxicity of the drug becomes thus one of great importance in any assay of the relative merits of anti-rheumatic agents. Toxic reactions of varying severity have been reported in almost every account published in the medical journals of Europe and America, their frequency varying with the dosage used and most often occurring when the daily dose has exceeded 600 mg. Among the serious complications are sodium and water retentions leading to oedema and sometimes also congestive heart failure. Fatal agranulocytosis in a case of rheumatoid arthritis treated with BTZ for 7 weeks (200 mg. thrice a day) was reported by Etess and Jacobson (*J.A.M.A.*, 21.2.1953). A case of multiple gastric ulcers occurring during BTZ therapy was reported by Raffensperger (*J.A.M.A.*, 2.5.1953).

Several reports have appeared in the medical press attributing gastro-intestinal bleeding to BTZ. Shields *et al* (*J.A.M.A.*, 2.5.53) added a case of duodenal ulcer bleeding and two cases of perforations of gastric and duodenal ulcers during BTZ therapy. Massive hæmorrhage occurred in a case of gastric ulcer, following the use of BTZ (*J.A.M.A.*, 152: 1; p. 31). Steinberg and his associates, report the death of a 52 year-old-woman who had rheumatoid arthritis over a 15 year period and who received 400 mg. of BTZ daily for 26 days and died as a result of agranulocytosis, though several patients with musculoskeletal disorders have received BTZ therapy without such a dire result. In the series of 140 patients treated by Kuzell *et al*, one patient had an unexplained massive hæmoptysis and subsequently he developed severe secondary anæmia. There was no instance of leucopænia in their series. Loxton and his associates (*Lancet*, 2: p. 682, 1952) reported one case of complete agranulocytosis in a series of 50 cases treated by them with BTZ. Two additional cases were since reported in a subsequent issue of the *Lancet*. So far, atleast 4 deaths from agranulocytosis attributable to BTZ have been reported. (*Br. Med. Jour.*, 1952, ii,

p. 1427; *Lancet*, 24-1-53; *J.A.M.A.*, 153:33, *J.A.M.A.*, 1953; 639) Dilling, (*Lancet*, 20-6-1953) adds another case to this list of four. BTZ bears a structural similarity to amidopyrine, a drug known to have caused agranulocytosis many times. A history of peptic ulcer or dyspepsia should put "the physician on his guard, because of the risk that BTZ may induce gastro-intestinal hæmorrhage and even precipitate heart-failure. The patient must be warned to watch for and promptly report the onset of purpura or any other signs and symptoms which may herald agranulocytosis e.g., malaise dryness of the mouth, fever, sore throat etc. The dose should never be allowed to exceed 600 mg. in twenty-four hours."

Opinions of different observers vary widely as regards the incidence and severity of the many side-effects produced during the course of BTZ therapy. Commenting editorially on the risks of BTZ therapy, the *British Medical Journal* of 13th June 1953 says "It seems probable that the variations noted by different observers (1.8 to 52%) in the toxic reactions is a reflection of the difference in the observers or in the conditions of observation. If so, too much attention should not be paid to a percentage of toxic reactions as an indication of the risks of using this drug". In his letter published in the *B.M.J.* of 20-6-1953, Dr. Wilson however, states that he found the drug to have a deleterious effect in a case of quiescent tuberculosis of the left lung and so he advises great caution in its use. ENGLEMAN found (*Ann. Rheum. Dis.*, 1952; 11: p. 259) that serial biopsy of rheumatic nodules revealed no change in the microscopic appearances as a result of the treatment; no constant fall in sedimentation rate accompanied the treatment with this drug. Dr. Rhys Davies and his colleagues found no change in the sedimentation rates.

The *Lancet* of 20-6-1953 says "If granulopænia is a manifestation of drug allergy—and with amidopyrine (to which BTZ is chemically related)—prolonged or repeated treatment may be expected to favour its occurrence. How this aspect of sensitization is related to dosage is obscure. In these circumstances BTZ should *not* be used merely as an alternative analgesic in rheumatism. Careful selection of patients and close attention to signs of toxicity are now rightly demanded; and it is therefore, questionable whether these conditions can be fulfilled without hospital supervision." The toxic potentialities of BTZ will have to be determined from a still larger number of observations by many more experienced observers. The comparative safety of continuing administration of the drug for an indefinite time in these chronic painful conditions, can be decided only on the basis of further extensive observations and until additional information and greater experience are gained, BTZ may be prescribed only with due regard for its known reactions and our present incomplete knowledge of its "metabolic and other long-range reactions and possibly untoward effects."

MEDICINE AND THERAPEUTICS

**A new long-acting insulin.**—(B.M.J., 31 Jan. 1953, pp. 242-244 and annotation, p. 266).

Vast improvements have been made in the manufacture of insulin subsequent to its discovery in 1921. The ordinary insulin has a quick action, which is over in 8 to 10 hours, thus necessitating a second dose in 24 hours, to control the blood sugar after the evening meal and during the night. As a result of many attempts to prolong the action of insulin, two well-known preparations combining zinc in their make up have come into use, i.e., protamine and globulin insulins. The action of these two is slow at the beginning but may last for 20 to 26 hours, so that the fasting value of the blood-sugar may remain within normal limits. The slow onset of the action of protamine zinc insulin is overcome by mixing it with some of the ordinary quick-acting insulin; this gives good results but entails either two separate injections or measuring the two insulins in one syringe. Some patients find difficulty in doing this. In November 1952, Hallas-Møller, Petersen, and Schlichtkrull (*Science*, 1952, 116: 394) described a new modification of insulin which appears to possess many advantages. They found that the addition of protamine or globulin to make the insulin insoluble was unnecessary, since it could be achieved by using a neutral acetate buffer with the addition of 2 mg. of zinc per 1000 units. Crystalline insulin cannot take up more than 0.8 mg. zinc per 1000 units but this new insulin in some way is made to take up 2 mg. zinc. Its action depends on the amount of amorphous insulin present, since this has a quick action on the amount of crystalline insulin having a slow action and on the size of the crystals, since large crystals have a long delayed action. The Novo laboratories in Copenhagen (Denmark) have now made three preparations "the semi-lente", "lente" and "ultra-lente", the first having the shortest and the last the longest range of activity. Law-

rence and Oakley gave "the lente" insulin to 11 adult patients who all had a severe type of diabetes; six were men and 5 women, their ages varying between 25 and 92. Some of these patients were having 2 doses of soluble insulin, some one dose of protamine zinc (P.Z) insulin or globin insulin and some a mixture of soluble and P.Z insulin. When the diabetic condition was reasonably stable under this treatment the blood sugar was estimated four times a day. The patients were then changed over to a single daily dose of "lente" insulin (the amount of insulin remaining the same) and 2 days later the blood sugar was estimated at the same time as before. The figures differed from case to case but in the individual patients the four blood sugar values after injection of "lente" insulin were roughly similar to those obtained with the other insulins. The injections were well tolerated and the liability to hypoglycaemia was slight. As only one injection a day of this new insulin is needed, it is worthy of further trial; and if it produces more constant results than mixtures of P.Z insulin and soluble insulin it will be much appreciated.

**Bell's palsy and stellate block.**—(J.A.M.A., 150, 1952, pp. 32-33.)

Bell's palsy is not a serious disease and recovery is spontaneous in the vast majority of cases; this recovery is however, long delayed in many instances, and the cosmetic effect of altered facial appearance is psychologically distressing. Time may be lost from work, because of this. Over 85% of all cases fall into the idiopathic aetiological group. Exposure to cold or draughts, otherwise known as refrigeration has been considered an important factor, though it has been determined in only a small percentage of a large series of reported idiopathic cases.

Two patients with complete idiopathic facial paralysis were treated by repeated homolateral stellate ganglion procaine hydrochloride

blocks, that were instituted soon after the onset of the palsy. The function returned much more rapidly than could have been expected in the natural course of the disease even with the best previously known therapeutic measures. This suggests a possible important vascular aetiological factor. Dr. Swan reports successful results on two more cases since the publication of the results on the first two patients.

**Sodium fluoride therapy in filariasis.**—(Subramaniam, R., *Jour. Ind. Med. Assoc.*, 22: 9, 1953).

The treatment of filariasis is still in a very unsatisfactory state. Particularly for the elephantoid leg and scrotum, medical treatment so far available is very poor. In 1945, the late Dr. Venkateshram Pillai, Prof. of Pharmacology in the Madras Medical College, noted that the incidence of filariasis was nil in places where fluorosis was endemic. This made him try sodium fluoride for filariasis. He made a 1 per cent solution and administered it orally. At his suggestion, I tried the same as injection. The result though encouraging was not then taken up seriously.

Last year, owing to the unsatisfactory results of treatment of filariasis I once again started giving in a case of well-marked swelling, sodium fluoride 1 per cent 1 c.c. subcutaneously, once a week, for four weeks. At the end of 4 weeks' treatment, no further injections were given for one month and again another course was given. In some cases smarting pain used to occur soon after injection lasting from a few minutes up to half an hour. In no case was the pain so severe as to necessitate discontinuing the treatment. In some other cases, after the first injection there was a tendency for the latent condition to flare up. In still others it induced filarial fever or lymphangitis. Since this reaction was observed regularly, sodium fluoride therapy was preceded by the administration of sulphadiazine 1 gm. three times a day for a week. In some other cases one course of Hetrazan or Bano-cide tablets was given. After this regime was started, no reaction was observed

in any of the cases. The treatment outlined above was given to 16 patients and it was observed that as injections progressed, the swelling came down and at the end of the 4 injections, the swelling was definitely less than at the start. After 4 injections, no further injections were given. The patient was asked to report once a fortnight to observe the condition. If at the end of three months the swelling was still present, another course of 4 injections was given as at the beginning; provided the swelling was only moderate in size i.e., up to 3 times the normal leg, it was reduced to the size of a normal leg. In cases of gross swelling, there was not much appreciable effect noted. Even if no appreciable effect was noted, the patients observed that the fever which they used to get periodically at the commencement of this treatment, had ceased. They also felt better after the course of treatment was over. It is not possible to say how far, a psychological element was responsible for the sense of well-being at this stage.

In two cases of hæmatochyluria, both of more than a year's duration, sodium fluoride therapy was tried. There was gradual improvement as the injections progressed and at the end of the 4th injection, hæmaturia and chyluria in both of them disappeared. In the first case it is now three months since the cessation of treatment. In the second case it is now two months since the treatment was stopped. Yet both are free from the complaint. It is as yet too early to say how long they will maintain the improvement. In the absence of satisfactory treatment for this condition and in view of the good results obtained with sodium fluoride, this is worth trying in this complication of filariasis.

In a case of filarial scrotum, after the second injection, the patient had fever for sometime and it turned out to be a filarial abscess of the scrotum which responded very well to sulphadiazine, incision and drainage. Thus the main drawback of sodium fluoride seems to be the tendency to precipitate a reaction. Preliminary treatment with sulphadiazine, will prevent this. The local pain at the site of injection is lessened by diluting the solution to 2 c.c.

with distilled water or by adding i.c.c. of 1 per cent novocaine. All the cases included in the table are cases in which the swelling had lasted for some years and had failed to respond to other lines of treatment. Though some others have claimed Hetrazan as having brought about reduction in the filarial leg, it had no effect in any of my cases. Where the filarial swelling had lasted for more than a year Hetrazan or similar drugs have no effect on the swelling. It is for these cases that sodium fluoride is most valuable. In a small percentage of cases, on the day following the sodium fluoride injection, patients complained of stiffness in the limbs, particularly in the shoulder region.

The treatment suggested above is a very simple one and is also very cheap. Filariasis is highly endemic and affects extremely poor people who cannot afford costlier treatment like Hetrazan. Sodium fluoride may be given to them after administering sulphadiazine for five days. Some of the cases have been followed up now for two or three years without a recurrence of the swelling. The amount of sodium fluoride administered to secure therapeutic response is not likely to induce any toxic symptoms of fluorosis.

#### Removal of radioactive contamination from hands.—(*Br. Jour. Indust. Med.*, London, 10 : p. 32, Jan. 1953).

An investigation was designed by Gregory to determine the comparative value of certain washing agents in removing radioactive contamination from worker's hands and was carried out in a factory processing radioactive materials. Those working in contact with radioactive materials are provided with a complete change of clothing to be worn in the factory. On completing the day's work employees remove the special factory clothing and pass through a shower bath. Their hands are checked on machines to determine their degree of radioactive contamination. This has come to be known as "hand monitoring" which is carried out on an "alpha" hand-counting instrument. If any contamination above a certain maximum

permissible level is discovered, the hands are washed again until the contamination has been removed. Maximum permissible levels of hand contamination for alpha activity is 600 counts per minute per hand. For 10 months preceding October 1950, a large number of hand-monitoring checks were carried out on employees of this factory and 1.5% of the process workers showed some detectable radio-active contamination. In only 0.22% was the contamination greater than 600 counts per hand per minute. Ten cleansing agents were compared by Gregory and of these white "Windsor" soap and a mixture of equal parts of soap-powder and wood flour were found to be the two most effective for cleansing the hands of substances containing uranium and radium. —(*Abst. J.A.M.A.*, 152 : May 1953).

#### Procaine amide.—(*Br. Med. Jour.*, 31-1-'53, Annotation).

This has been used during the last few years in treating arrhythmias and other heart irregularities. The Council on Pharmacy and Chemistry of the American Medical Association, whose reports are usually conservative and trustworthy, points out that it depresses the irritability of the ventricular muscle, having a more prolonged action than procaine and one-half to one-third the toxicity. It can be taken by mouth, and it is useful in treating ventricular arrhythmias and extra systoles occurring in heart disease or during general anaesthesia. If given intravenously it causes a fall of blood pressure. Mason and Pelmore in their preliminary report (*B.M.J.*, 31-1-'53) describe a new use of procaine amide in conjunction with hexamethonium to lower the blood pressure in maxillo-facial and other operations and so to allow the surgeon an unobscured field. When procaine amide was given after hexamethonium in 2 cases, the effect which they obtained was a slowing of the pulse-rate, which might have been due to a direct action on the heart or to exclusion of the rise in rate caused by a fall of the blood-pressure. It will be interesting to learn whether this procedure is adopted by other anaesthetists.

Shack, Hoffman, and Vesell (*Br. Heart Jour.*, 1952, 14, p. 465) and Lucas and Short (*Br. Heart Jour.*, 1952, 14, p. 470) have used procaine amide for cardiac irregularities. Lucas and Short found that the intravenous administration was more effective than giving by mouth, and by the intravenous route they were more successful in arresting ventricular tachycardia in 4 out of 5 cases and ventricular extra systoles in five out of five cases. Supra-ventricular tachycardia and extra-systoles were confined to gastrointestinal upsets, and hypotension.

Davis (*New. Eng. J. Med.*, 1952: 247, 673) described the successful treatment of a case of angina pectoris brought on by exercise and accompanied by pulsus bigeminus. The patient was given 0.25 g. of procaine amide at 4-hour intervals and remained free from anginal attacks for 16 months. Goldman (*Am. J. Med. Sci.*, 1952: 224, 573) has treated hereditary or Huntington's chorea with procaine amide. Its use in this condition was due to a chance observation that a patient sitting in a dentist's chair had little or no choreiform activity after an injection of procaine for the removal of a tooth. The effect of procaine amide varied with different patients, though all benefited to some extent and a few got completely cured of chorea. A large dose, 1.0 g. four or five times a day was used and this was tolerated only by raising the dose gradually during 2 or 3 weeks from an initial dose of 0.025 g. The immediate use of a large dose caused somnolence and feelings of faintness and numbness. As there has been no treatment so far for this form of chorea, these results sound hopeful.

**Aperients in chronic constipation.**—(Sir Adolphe Abrahams, *Practitioner*, March 1953, pp. 269-270).

Although the therapeutic ideal is to make the sufferer from chronic constipation independent of all aperients and purgatives, except in an emergency, there are definite indications for their use. They will be required during the process of re-education or to

supplement muscular inadequacy of the gut which often follows serious illness: also in intractable senile conditions, or to ensure a soft stool to avoid pain in anal fissures, or inflamed piles, and when coma threatens a diabetic, or to prevent straining at stool in myocardial or arterial disease. During pregnancy and puerperium also, they may have to be used routinely.

*The choice of the aperient:*—The choice of one intended for continued or possibly unlimited, use calls for great circumspection. It should be such as no increase in dosage, rather the contrary, will be necessary.

*Saline laxatives* act essentially by preventing normal absorption of water. Obvious disadvantages exist in producing fluidity of the intestinal contents.

*Liquid paraffin:*—As this is taken as a routine on a very large scale, Sir Adolphe Abrahams of the London Westminster Hospital has examined its virtues and disadvantages in a very interesting and informative article on "Chronic Constipation". It is regarded as a bland innocuous intestinal lubricant mechanically softening the stools and stimulating peristalsis to some extent. Some credit it with having the property of absorbing and filtering toxins. The comparatively minor disadvantages are gastric disturbances, nausea, and regurgitation, borborygmi and intestinal discomfort and pruritus ani. Seepage from the anus will doubtless produce embarrassing consequences. These objectives and inconveniences may be prevented to some extent by taking the oil before food or mixing it with 'kaylene'. The more serious disadvantages are: Interference with the normal process of defaecation. Leakage from above, results in the rectum being continuously partially full, its volume not exercising sufficient to initiate the defaecation reflex but enough to cause irritation. There is evidence of interference with digestion by increasing the rate of passage of the contents of the small intestines and by coating the intestinal mucosa, so preventing secretion and absorption. Owen in 1932 (*S. Afr. Med. Jour.*, 6: 87)

cited 34 cases of adult women who lost weight and became weak as a result of regularly using liquid paraffin. Till (*J. State. Med.*: 42: 1934) and Zaborsky (*Arch. Paed.*: 60: 250, 1943) recorded similar experiences in children. The system is depleted of the fat-soluble vitamins, according to Curtis (*J.A.M.A.*, 113: 1785, 1939). Some manufacturers alive to this disadvantage have added vitamins to their preparations. Liquid paraffin is *not* suitable for regular administration to pregnant women and to those undergoing surgical operations, as there is danger of hypoproteinaemia, in addition to malnutrition. (Javert and Macri (*Am. J. Obst. Gynaec.*, 42: 409). Paraffinoma of the lung has occurred from regurgitation in old and debilitated persons compelled or restricted to recumbency and in others with neurologic damage predisposing to the entrance of the oil into the trachea and also in apparently normal people. A carcinogenic property has also to be finally mentioned as a possibility, though as yet is has not been regarded as of serious import.

*Phenolphthalein* has much to recommend it; it is tasteless and forms a soluble salt in the intestines stimulating peristalsis in the colon without producing griping. It is excreted slowly so that a single dose often, has a prolonged action over 3 or 4 days. It fell into disrepute on the charge of creating renal and hepatic damage, but extensive researches by Fantus and Dyniewicz (*J.A.M.A.*, 108: 409 and *Am. J. Digest. Dis.*, 8: 176) have exonerated it.

*Senna* has a long and honoured reputation for over 1000 years. It is the most desirable of the anthracene group of drugs which include aloes, rhubarb and cascara. 'Senna tea' is a domestic remedy prepared by soaking the *Pods* (not leaves) in cold water for a whole day and drinking the infusion at night. Syrups, tinctures, confections, powders and extracts, made from the leaf, not the pod, are official preparations. The leaf contains a resin with griping properties. The glycosides of senna are absorbed in the small intestine, to be slowly excreted into the large, where by bacterial action a substance is produced that stimulates peristalsis through Auerbach's plexus. There is thus a good reproduction of the physiological process of normal defaecation.

*Hydrophilic colloids*: A different type of aperient comprises the inert mucilaginous substances, the essential of which is the insoluble protein (bassorin, a tasteless odourless vegetable gum) of tragacanth and acacia. This action is hygroscopic and on reacting in the intestine a soft pulpy mass is produced with a purely mechanical action. Familiar preparations of this type are:—'isogel', 'normacol', agar-agar, and visiblin.

*Thyroid extract*:—In inveterate cases, thyroid extract is sometimes effective owing to its action on the sympathetic nervous system.

*Physico-therapy*:—Massage and abdominal exercise also play a useful part.

## SURGERY

**Treatment of keloids.**—Dr. Bethel, Solomons, Jr., Dermatologist, Dr. Steeven's Hospital and the Royal City of Dublin Hospital, discussing various methods of treatment of this troublesome condition divides the treatment into (a) prophylactic and (b) curative.

Prophylaxis is thought to play an important part in the treatment of keloids since the majority of keloids are post-operative in nature. The post-operative keloids, otherwise known

as scar-keloids may be prevented by observing certain precautions during operation like making incisions parallel to or in the creases of flexion. An additional prophylactic measure may be the combined use of pre- and post-operative irradiation. For this purpose the author recommends the use of Levitt's technic of X-ray exposure which consists of the use of (1) a low voltage as much as 50 to 80 kilovolts (2) given at the shortest possible treating distance with (3) minimal surface area exposure

obtained by an accurate close covering with lead sheet (4) the dose to be adjusted to produce a faint erythematous reaction, i.e. a first degree reaction with an interval between the first and second exposure of not less than 2 weeks.

The curative treatment of keloids involves the use of carbon dioxide snow to the area of keloids. The author follows the method used by Solente who begins with applications of two-pound pressure for 10 to 20 seconds, and continues weekly until a time of 50 seconds, or the disappearance of the keloid has been attained. Marshall and Rosenthal had success following the parenteral injection of a special fraction of liver extract known as Kutapressin. The most effective form of therapy however is again the use of X-rays. Radium is not of much use, but deep X-ray therapy has been found to be very effective. This treatment, should be left to radio-therapists. The hard area of the keloids gradually become soft and pliable after involution of the keloid following deep X-ray. Certain old and thick keloids could be removed by excision or electro-surgery combined with radiation. The use of ACTH and allied substances are still in the experimental stage and the results are not yet very clear; these may however, play an important role in the treatment of keloids.—*Practitioner*, May '52, pp. 470-472.

**Lumbar Sympathectomy in the treatment of peripheral vascular diseases.**—(*Surg. Gynaec. Obst.*, Chicago, 96, Feb. 1953, pp. 162-163).

Palumbo, Quirin and Conkling report the effects of lumbar sympathectomy in the treatment of peripheral vascular diseases in 159 male patients upon whom 221 operations were performed from October '46 to December '51. This study included the following diseases or conditions: arteriosclerosis (including diabetics), arterial emboli, aneurysm or thrombosis, Buerger's disease, freezing, immersion foot, causalgia, chronic throm-

bophlebitis, varicose or chronic leg ulcer and peripheral vascular disease of undetermined type or cause. The patients ranged from 20 to 84 years of age, the average age being, 45.5 years. Fifteen per cent of the patients were over 60 years of age. The results of the entire series were considered good to excellent in 65 per cent and fair in 28 per cent. The greatest number of patients who were benefited by the procedure were those with Buerger's disease, varicose or chronic leg ulcers, and those who had freezing, immersion foot, or causalgia. The patients who had arteriosclerotic disease of the peripheral vessels, even though their average age was greater than the above groups revealed results which were considered good to excellent in 60 per cent of the cases. Thirty-four per cent of the patients with chronic thrombophlebitis obtained good to excellent results following sympathectomy. In addition, 48 per cent were slightly improved following surgery. The complication rate was less than 10 per cent in the entire series. The favourable results are based on improvement of circulation of the extremity due to release of vasospasm and development of smaller collateral channels of the vascular bed not involved by the disease process. Lumbar sympathectomy, in properly selected patients with the diseases or conditions studied showing a vasospastic element and an elastic potentiality of the vascular bed, resulted in early relief of symptoms, rapid healing of ulcers, diminution of oedema, subsidence of cellulitis. It also prevented or delayed the need for a major amputation in many cases so that many limbs which, by former standards or methods of treatment would have been sacrificed, were saved. If amputation becomes necessary, frequently it can be performed at a lower level with safety, and rapid healing will usually ensue in the majority of cases.

This method of management has resulted in early rehabilitation of many patients and has considerably reduced their period of hospitalization.

## OBSTETRICS AND GYNÆCOLOGY

**Dysmenorrhœa.**—(*Am. J. Obst. Gynec.*, March 1953).

The fact that primary dysmenorrhœa tends to decrease with increasing maturity and/or following pregnancy and the birth of a full term infant lends additional weight to the idea that this transient syndrome is in fact the product of a dysfunctional union between the myometrium, the uterine vascular bed, and their chemical or hormonal regulators. The dual mechanism not only accounts for the variable discomfort characterizing dysmenorrhœa but also explains the capricious result obtained with contemporary therapy. In primary dysmenorrhœa, the administration of antispasmodic drugs to control hyper-contraction of the uterus and vascular spasm are expected to bring relief.

Rest in bed, and use of heat are the oldest and commonest remedies for menstrual discomfort. Their usefulness is sometimes overlooked by young male physicians whose knowledge regarding menstruation in general, and dysmenorrhœa in particular, is usually, tenuous. While suitable for young adolescents not subject to social inconvenience or economic loss, such periodic disablement becomes objectionable or impossible for adults.

The use of a positive pain-relieving drug such as codeine presents several problems. While its employment is widespread, its use is generally preceded by a good deal of bush-beating, and sensibly so. Preliminary trial with remedies containing acetyl salicylic acid or phenacetin in various combinations are to be recommended. They may give adequate relief and circumvent objections accompanying the use of a stronger drug or opiate, when these common

remedies fail, the use of codeine alone or in combination with stimulants such as caffeine or sedatives such as phenobarbital, will serve as an effective means for achieving pain-relief. We favour the oral use of codeine not only because this is more convenient, but also because it is psychically better for the patient and ethically less disparaging to the medical profession. While codeine should not be prescribed unless necessary, we believe the hazard of habituation to be negligible from the monthly use of small amounts for the relief of incapacitating dysmenorrhœa.

Since primary dysmenorrhœa does not occur in the absence of ovulation, the prevention of ovulation by the administration of adequate amounts of oestrogen or testosterone during the first half of the cycle represents a positive method for providing relief. However, this method also has its limitations. It is probably unwise to prevent ovulation for many months in succession. Perhaps this caution is unnecessary. Possibly time and experience will reveal that ovulation may be inhibited for months without harm to the patient or interference with the return of ovulation when this is deemed desirable. Until we can be assured regarding these points, however, this method should be utilised for restricted periods of time only. The use of the male hormone to prevent ovulation has the added objection that in some instances its use causes hirsutism and occasional voice changes; while these manifestations commonly disappear upon discontinuance of the drug they do not always do so. While surgical procedures have a place in our therapeutic armamentarium they are to be looked upon only as a last-resort measure.

## REVIEWS OF BOOKS AND PERIODICALS ETC.

**A Treatise on Hygiene and Public Health**—By B. N. GOSH, 13th Ed. 1953, pp. 787. Scientific Publishing Co., 85, Netaji Subhas Road, Calcutta 1. Price Rs. 17/8- or 25 sh. 6 d. This very useful treatise on Hygiene

and Public Health has reached its thirteenth edition in 1953. The fact that it has done so in 40 years, clearly indicates its popularity amongst medical students for whom it is primarily intended. Dr. Gosh has spared no pains

to revise the book and bring it up-to-date in every successive edition, and in the present one he has incorporated much new material, which was not contained in former editions. Thus, new monographs on poliomyelitis and infantile cirrhosis of the liver, and a detailed account of the activities of the WHO have been included. The monographs on Relapsing Fever, Typhus Fever, Beri-Beri, and Epidemic dropsy have been revised by Sir John Megaw. The chapter on Vital Statistics has been revised and brought up-to-date by Mr. S. P. Jain, the well known statistician to the Labour Bureau of the Govt. of India. Recent advances on various subjects connected with Hygiene and Public Health, like the Treatment of Rabies, Maternal Mortality, Dietetic Diseases have all been duly incorporated under the proper headings, having been revised and supplemented by specialists in the particular branches of knowledge. The latest modern insecticides, their usefulness, fields and modes of application, have also been included in this new edition. In fact every one of the 29 chapters has received a thorough revision in the light of modern advances in knowledge and technique. The chapter on Social Medicine, envisages the implementation of a fairly comprehensive policy for India along three lines viz., the development of social services including health insurance, the work of slum clearance to provide a minimum standard of housing and the inauguration in medical colleges of social medical services, on approved and useful lines.

This valuable text book is complete and comprehensive and so would continue to meet the needs of the modern medical and public health students and also of all public health workers.

T.N.S.B.

**The Medical Annual—(A Year Book and Practitioner's Index)—**Edited by Sir HENRY TIDY, K.B.E., M.A., M.D., (Oxon), F.R.C.S., and A. RENDLE SHORT, M.D., B.Sc., F.R.C.S., 1953. (Bristol: John Wright & Sons Ltd.). Price 27sh. 6d.

The Medical Annual has now entered its seventy-first year of publication;

and we notice a welcome change in its appearance and get-up which marks a great improvement over former editions. The type face is now larger in size and we are glad to note an all round improvement in general and typographical arrangement. As usual the Medical Annual supplies the busy practitioner with crystallised information on all outstanding advances that have been achieved during the previous years, in all branches of medicine and allied subjects, both as regards diagnosis and treatment and also other relevant matters. Recently introduced drugs, medicaments, surgical and other appliances have all found a place in the annual.

The contributors to the annual are all top-ranking men of outstanding ability and reputation in their respective fields and have done full justice to the topics which they have set themselves to discuss. The opening article by the medical historian Dr. Charles Singer on "Medicine in the Reign of Queen Elizabeth I" furnishes very interesting reading. Dr. Bradley writing on diphtheria warns practitioners against the dangers of the exaggerated claims made about the efficacy of immunization, as the ultimate good results obtained in certain cases may have been due to other factors at work. The contribution on the use of ACTH and Cortisone in various conditions and the review on Disc herniation, are indeed so very elaborate and instructive as to provide valuable and up-to-date information to the general practitioner.

Among the numerous other topics dealt with in the Annual for 1953 are Anæmias, Antibiotics, Anæsthesia, Intra-arterial transfusion, Burns, Cardiac Surgery, Diabetes, Gall-bladder Surgery, Mental diseases, Rheumatic Conditions, Thyroid gland and its surgery, Radio-therapy, Poliomyelitis, Legal decisions and Legislation, Veterinary medicine in relation to human medicine, etc. The Medical Annual has for several years rightly been considered a prized possession of every practitioner of medicine and the present issue, is no exception. It marks also a definite improvement on the previous ones. Medical practitioners who wish to keep abreast of modern achievements and

advances in all fields of medicine will find this annual to be a handy source of information and help in their daily work.

T.N.S.B.

**Bulletin of the National Society of India for Malaria and other Mosquito-Borne Diseases. (Vol. I., Nos. 1 and 4, 1953).**

We have received from the Secretary of the above Society copies of their Bulletin for January and July 1953.

In her message dated 16.1.53, the Union Health Minister stated: "Malaria is a national public health problem of prime importance. The creation of a National Society for combating Malaria and other mosquito-borne diseases is both timely and useful". Modern methods of malaria control aim, "*at an immediate objective to achieve a quick elimination of the problem by repeated application of potent insecticides and a long range objective of permanently eliminating the breeding places for mosquitoes by filling, drainage etc*". The National Malaria Control Programme, is a comprehensive one as set forth in the first issue of the Bulletin published in January 1953. It is unique and is an unprecedented venture which is designed to afford protection

from malaria to a huge population of about 125 million people and has already started functioning, with the united co-operation of the Union Government, WHO and UNICEF.

Col. Jaswant Singh, Director of the Institute in an informative article on Malaria and its control; details the preventive and curative work undertaken by the Government and the Indian Council of Medical Research since 1908. Srivastava, Chand and Singh describe the measures for controlling malaria adopted in various districts of Uttar Pradesh. The scope and limitations of residual insecticides in malaria-control are discussed by Sharma of the Malaria Institute. Gilroy of the Ross Institute of Tropical Hygiene, India and Pakistan Branch reports on the success of the control measures in the Anamalais and the planting districts of Wynad. Residual insecticides alone, in his opinion, will be sufficient and proguanil reinforcement of DDT or BHC is not necessary. Malaria-control in West Bengal consisted of anti-adult and anti-larval measures, and distribution of antimalarial drugs.

The Bulletin furnishes very valuable information which will be of use to all workers in this field.

T.N.S.B.

### BOOKS RECEIVED

The following books have been received with thanks since 15-8-'53 and the courtesy of the publishers in sending them is acknowledged. Reviews will appear in due course—Ed.

1. **Incompatibility in Prescription**—Sixth Edition. By Dr. JAMES

BURNET, M.A., LL.B., M.D., F.R.C.P.E.,  
The Prescriber Publishers Ltd., Edinburgh, 1953.

2. **Ayurvedic Flora Medica**—By VAYASKARA N. S. MOOSS. Messrs Vaidyasarathy Press, Kottayam. 1953. Price Rs. 12/-.

### CORRESPONDENCE

I

To the Editor, ANTISEPTIC, Madras.  
Sir,

I read with pleasure and profit the article on the "Treatment of Typhoid Fever" by Dr. Subramaniam, in the issue of ANTISEPTIC, August '53.

He has used Chloramphenicol, Synthomyecin, Cortisone and ACTH

They are all costly drugs. India is a very poor country where 62% of the people, have to incur debts every month to meet the daily essential expenses for food, shelter and clothing. Under such circumstances, costly drugs are impossible for general and routine therapy. They may be all right for treating the rich. Chloramphenicol

and Synthomycin act more like policemen who keep the offenders in custody; they are only "bacteriostatic". They have not solved the problems of "relapses" (8%) and "carriers". They may be good for large hospitals where the supplies are sent free by the manufacturers for purposes of advertising their preparations.

In any fever, the liver is the first organ of digestion to go out of order. I do not see how patients will be able to digest fatty foods—butter, curds, shark or cod liver oil etc. Therefore, it is routine to keep a fever patient on liquid diet—butter-milk, milk (without cream) mosambi juice (for Vit. C) etc. Tea, Coffee. The "American" full diet gives rise to severe diarrhoea. In "Typhoid" we want some "bactericidal" specific drug, like quinine for malaria or 608 or 914 for Syphilis.

May I earnestly request Dr. Subramaniam to carry on researches in this direction and discover some bactericidal drug at once cheap and effective and within the reach of the very poor people of India?

Nandurbar. } (Sd.) NANDALAL B. VANI,  
31-8-'53. } M.B., B.S.

Shri Dr. R. Subramaniam, to whom we referred Dr. Vani's letter writes to say in reply: "I agree with Dr. Vani that India is poor and a large percentage of the population have to eke out a hand to mouth existence. Even so, human life is precious and a man should not, merely on the ground of poverty be denied proper treatment irrespective of the cost of the drug. Are we not treating cancer with radium which is much more costly? The remedy really lies in finding ways and means to provide the suffering man with the drug that is necessary by private and public munificence and from state aid. With regard to relapses, I have myself outlined a cheap method of controlling them by administering T.A.B. vaccine. Cortisone or A.C.T.H. is administered only for 4 or 5 days. Cortisone tablets at the rate of one tablet three times a day for 5 days will mean anywhere between 10 to 12 tablets of 25 mg. each. The cost of this at the existing market rate will be about

Rs. 20. Surely this is not much considering that the fever period is cut down to less than 48 hours. I have not advocated butter or curds during the fever period, but only after convalescence has started. With regard to shark liver oil or cod liver oil, it is not given as oil but only as an emulsion, for its calorific value. I have used this as a routine for the last 14 years, during which the routine microscopic and macroscopic examinations of the motion have revealed no fat or fat globules. I have not advocated anywhere in my article the American full diet. With regard to the suggestion of discovering some drug which is bactericidal, a large team with considerable financial aid is necessary for this research. Under the new set-up, Government have some proposals for aiding such a scheme and when we are given an opportunity we will certainly press for starting a bacteriological research scheme to culture various mycelial elements and find out one which will be bactericidal to typhoid bacilli without being harmful to man. The real bottle neck for research is finance!"

## II

To the Editor, ANTISEPTIC, Madras.

Dear Sir,

With reference to the letter of Dr. Sethu Rao published in the ANTISEPTIC of April 1953, I wish to suggest the following for his child.

The child has apparently a psychic and somatic imbalance. Any type of food irritating to the taste and to the stomach will not be tolerated.

He should start with "Dalia" of wheat prepared in milk; roast the wheat, then crush it to small particles and fry them in ghee; take 1 oz. of this, add 8 oz. milk and 10 oz. water; let it boil until it becomes homogeneous and is reduced to not more than 8 to 9 oz.; add glucose or sugar to suit the child's taste.

I have treated two cases on psychic lines; I had to get a few other children of the family to take tasty foods and biscuits in front of the defaulting child telling him that they would not give him, so that he might feel an

inferiority complex. He had to make up to adjust with other children. He begged me to give him something of that type but I, refused and when he became very eager then only I gave him toffee which was given to the other playmates.

He might try both these methods and she would probably begin to take the right foods easily without any reaction.

Aditya Pharmacy,  
Shahjahanpur,  
5th June '53.

DINESH C. DWIVEDI,  
A.M.S.,  
*Psychosomatic Physician*

### OBITUARY

#### The Late Dr. T. S. Tirumurthi

We deeply regret to record the death from heart failure of Sri Dr. T. S. Tirumurthi, B.A., M.B., & C.M., on the afternoon of the 28th August 1953 in a railway train between Bangalore and Mysore. He was aged 68.

Born at Udumalpet in Coimbatore District on 28th November 1885, he had a brilliant academic career. He entered the Madras Medical Service in 1908 and was Professor of Pathology for a long time in the Madras Medical College and also Third Physician in the Madras General Hospital. After serving as District Medical Officer for a short time, he was appointed Principal of the Govt. Medical College at Vizagapatam; later he acted as Vice-Chancellor of the Andhra University for sometime. He was the first Indian to be appointed as the Principal of the Stanley Medical College, Madras which post he held till the date of his retirement. He was elected President of the Indian Medical Association. He took a very keen and active interest in many social and educational problems and was also the President of the Governing Body of the National Educational Society, Triplicane, Madras.

He was unanimously elected President of the All India Medical Council

in 1952 at the Allahabad Session and with his rich and ripe experience of men and matters he guided the affairs of the Council energetically and well.

He was a member of the Senate and Syndicate of the Madras University for some time, as also of the Annamalai University. He was an able and enthusiastic supporter of all schemes and plans designed for the betterment of the medical profession. He was a facile writer and powerful speaker on public platforms.

He was one of the distinguished contributors to the Antiseptic and took a keen interest in his retirement in the advancement of the medical profession.

Simple and unostentatious in his habits, and of an exceptionally genial temperament, he endeared himself to all—patients, students and friends alike. He leaves behind him his widow, a daughter, two sons, four brothers (one of whom is Dr. T. S. Duraiswami, a popular Madras Eye Surgeon) and his son-in-law Mr. C. S. Ramachandran I.C.S., Deputy Secretary to Government, besides a host of friends to bemoan his loss.

By his death the Medical profession has sustained a serious loss. We offer our heartfelt condolences to the members of the bereaved family.

May his soul rest in peace!

### NEWS AND NOTES

#### Research Scholarships in Pædiatrics

The Association of Pædiatricians of India has resolved to offer two scholarships of the value of Rs. 1200/- each tenable for one year, for work on any Pædiatric subject or any subject allied

to Pædiatrics. Applications for these scholarships should be received not later than the 30th of September, 1953. For further information please apply to: The Secretary, The Association of Pædiatricians of India, Back Bay View, New Queen's Road, Bombay 4.

### CORRIGENDUM

ANTISEPTIC, August 1953, p. 601, for 'contracture significant' read 'contracture insignificant' under the heading 'Progress Sequelæ'.  
p. 601 for 'By degeneration' read 'By regeneration' under Results.



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References:

Amer. Heart J., 1949, 37, 531. Brit. Heart J., 1950, 12, 54.

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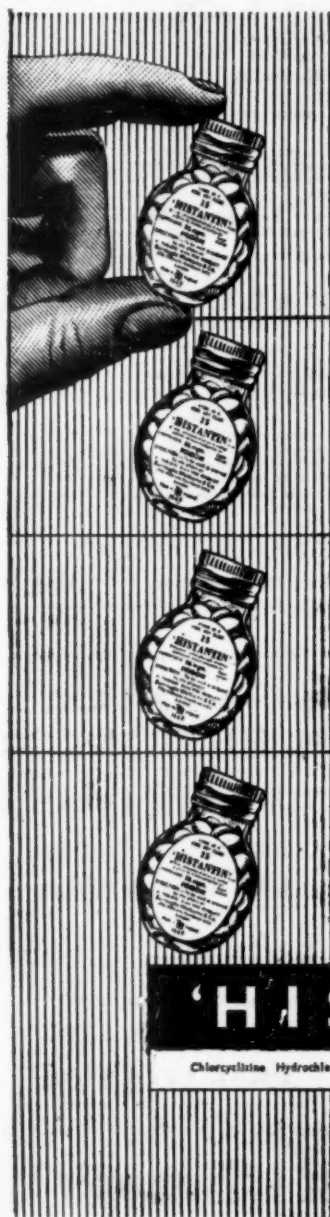
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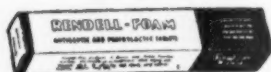


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### \*References

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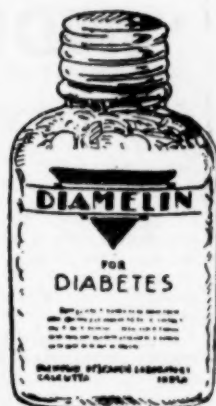
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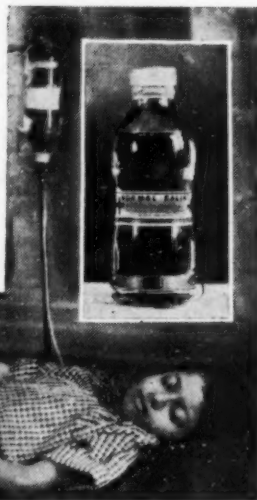
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\* "The superiority of 'Camoquin' over other antimalarials", Singh, I. & Kalyanum, T. S.  
Brit. Med. Jnl.

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